



RESEARCH ARTICLE

# Future implications of obesity, gestational hypertensive disorders and diabetes to health and longevity - the significance of lifestyle intervention

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## ABSTRACT

The association of obesity, gestational diabetes mellitus and hypertensive disorders of pregnancy are early warning to future compromise of women's health and longevity in the form of later life hypertension and overt diabetes mellitus and their complications, as was shown in some large population-based studies. The association of these two pathologies with maternal obesity is significant. The most efficient approach to preempt future consequences is a modification of lifestyle, leaning mostly on two pillars, dietary approach and physical activity, a comprehensive form of intervention that copes with all three, i.e. obesity, gestational hypertension and gestational diabetes mellitus. These interventions are discussed in this review as well as the most efficient ways of implementing them. All sources point to a major role for personalized approaches and some form of group support.

**Keywords:** Gestational hypertension, Gestational diabetes mellitus, Obesity, Lifestyle modifying intervention, Group support

**Abbreviations:** HT – hypertension, GDM – Gestational diabetes mellitus, GHTN – Gestational hypertension

## Introduction- A triple association between obesity, gestational hypertension and gestational diabetes

A growing body of evidence supports the major significance of gestational hypertension (GHTN) and diabetes mellitus (GDM) to the health and longevity of the affected women.<sup>1,2</sup> Herein we present a thematic review of the current state of knowledge on this issue and its association with obesity, leaning on recent literature deemed most relevant to the subject. We further consider the interventions deemed most appropriate to preempt these grave consequences.

Unlike men, women's physiology is challenged earlier in life by pregnancies during their reproductive years. In addition to the intrinsic importance of the latter pathologies to index pregnancy, pregnancies expose weaknesses in the individual woman's physiology, which have the potential of affecting their later life morbidity and longevity. A recent report on most singleton deliveries in Sweden during 1973 to 2015, encompassing 2,195,667 deliveries and 56 million person-years of follow-up, indicated that GDM and hypertensive disorders of pregnancy (including hypertension, preeclampsia/eclampsia and small for gestational age fetus/newborn) were associated with increased all-cause mortality of up to 1.5.<sup>3</sup> Two derivative studies from the same Swedish cohort found that within 10 years postpartum, women with both GHTN and GDM were about twice more likely to develop ischemic heart disease, a tendency that was maintained to the subsequent three decades.<sup>4</sup> It was also revealed that within 10 years chronic kidney disease was 7-fold more prevalent after GHTN and 3.5-fold after GDM, which was also maintained for the following 3 decades of life.<sup>5</sup> Thus, the same pathology which accounts for the heart and kidney conditions, namely atherosclerotic vascular disease, is the correlate of the two gestational conditions, GHTN and GDM. A study from the USA on a total of 91,426 parous participants, aged 34.9 (4.7) years, with a follow-up of 2,609,753 person-years, found

that women with a history of GDM had a 1.28 (95% CI, 1.13-1.44) higher crude mortality rate than those without. This trend was more pronounced among women who adopted less healthy lifestyles.<sup>6</sup> In this regard, Yang J, et al.<sup>7</sup> observed over a median 27.9 years of follow-up, that 924 women out of a cohort of 4,275 women who suffered GDM, developed type 2 diabetes, also explaining the observed increased rate of atherosclerotic consequences. The risk of developing type 2 diabetes was 90% lower for those women who kept optimal level of five modifiable risk factors (body mass index (BMI) <25.0, high quality diet, regular exercise, moderate alcohol consumption and no smoking).

Song X, et al.<sup>8</sup> used summary-level data from the largest available genome-wide association studies of five obesity traits, five lipid traits and GDM for two-sample univariate Mendelian randomization. They found that the odds of GDM increased 1.64-fold for 1-SD increase in BMI and 1.57-fold for waist-to-hip ratio. Beyond the genomic relations and genetic predisposition that increase the risk for GDM, patients with intestinal dysbiosis, mainly altered ratio of Firmicutes to Bacteroides and obesity, are at a higher risk of developing GDM.<sup>9</sup>

Obesity has a central role in predicting the odds for both GDM and GHTN. Song Z, et al.<sup>10</sup> found that pre-gestational BMI, and abdominal circumference were good predictors of GDM in a cohort of 15,472 pregnant women with a singleton pregnancy. In a cohort of 3,172 Chinese pregnant women overweight (OR: 2.80) and obesity (OR: 5.42) were risk factors for GHTN<sup>11</sup>. A cohort of 912 Polish pregnant women indicated the same tendency.<sup>12</sup> In a cohort of 2972 woman in Bahrain, out of which 1657 had BMI  $\geq 30$ , obesity increased the risk of developing GHTN 2.5-fold.<sup>13</sup> In a large-scale comparison of 555,446 Swedish and 79,243 Chinese pregnancies, obesity appeared as a strong risk factor for pre-eclampsia, more pronounced in China (OR - 5.12) than Sweden (OR, 3.49)<sup>14</sup>.

All the above, combined, strongly indicate that gestational pathologies in carbohydrate metabolism

or blood pressure are intimately connected to obesity, but nonetheless each of them has independent implications for later life health and longevity. The immediate issue that is raised by this constellation is the possible role of preventive measures to be taken upon the young-age occurrence of either obesity, GHTN or GDM.

## Lifestyle modifying interventions

Numerous modes of preventive interventions to safeguard future health were introduced to the fields of control for carbohydrate metabolism and hypertension. In the light of the clear association between obesity, GHTN and GDM the main concern is the compliance of young women with recommendations to alter their established eating and activity patterns. On one hand, the consequences may look remote from their life reality at present, but on the other hand pregnancy and the emotional atmosphere surrounding delivery of a new baby may help connect these women to even more remote consequences, thus helping to drive a change in lifestyle.

A significant concern is the way of recruiting women to participate in a concerted effort to change their habits, and the mode and framework of such an intervention. In this regard there are reports on experience with administering such programs and the rates of success in achieving their goals and the rate of adherence to the routine and retention in the program. Although many studies concentrated on either obesity or HT or diabetes mellitus, the triple-play, revealed by gestational circumstances, justifies pooling the insights of all these experiences into treating postpartum patients who were singled out by either of the three, namely, obesity, GHTN & GDM. Furthermore, all three are combated mostly by the same recommended lifestyle intervention.

Lifestyle means mostly diet and level of physical activity, in addition to refraining from smoking and alcohol, which is outside the scope of this review. Thus, we devote a chapter to each of the two foundations of lifestyle.<sup>15</sup>

## Dietary changes and restrictions

It was shown on multiple mammalian models that dietary restriction and limiting to specific contents affect health and longevity at various metabolic and molecular levels, which also contribute to prevention of multiple ageing-associated diseases in humans.<sup>16</sup> The major role of obesity puts the restriction of caloric intake at the top of the list. Yet, it appears that caloric intake should come second to the contents of the diet, since the contents entail the caloric load. Therefore, it is worth starting with the findings of a large meta-analysis<sup>7</sup> which revealed that Mediterranean diet adherence not only reduces gestational complications but also enhances fertility and gestational weight management. Furthermore, some studies suggested associations between higher Mediterranean diet adherence and later time to menarche and fewer vasomotor menopausal symptoms, attesting to later life favorable effects.<sup>7</sup>

Theodoridis X, et al<sup>17</sup> in a meta-analysis of 12 studies, found that both cohort and cross-sectional studies reported that high adherence to dietary approaches to stop hypertension diet was associated with a lower risk of developing hypertension compared to the low adherence. The largest and most recent meta-analysis, reporting 113 reports encompassing 3,277,684 participants, diets of the highest quality, as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, and dietary approaches to stop hypertension diet scores, were inversely associated with risk of all-cause mortality, cardiovascular disease incidence or mortality, and incidence of type 2 diabetes.<sup>18</sup> An umbrella review of 60 meta-analyses concluded that high consumption of Mediterranean and dietary approaches to stop hypertension, and interventions that modified the quality of diet intake significantly reduced risk of Type 2 diabetes mellitus especially in the high-risk population.<sup>19</sup>

## Physical activity

A prospective community-based cohort data of 5,115 participants with coronary artery risk development in young adults indicated that meeting approximately

twice the current minimum physical activity guideline level at age 18 years and through follow-up was protective of HT incidence.<sup>20</sup> In a large Chinese cohort of 9350 adults who were free of HT at baseline, moderate transportation physical activity was associated with lower risk of developing HT.<sup>21</sup> A recent large meta-analysis found that leisure-time physical activity reduces both systolic and diastolic blood pressure values in patients with an established diagnosis of HT.<sup>22</sup> Regarding formulated interventions, another recent meta-analysis showed that walking probably reduces blood pressure for all ages and both sexes.<sup>23</sup> Edwards JJ, et al.<sup>24</sup> in their meta-analysis showed that isometric exercise and running were the most efficient modes of physical activity in reducing BP. In another recent meta-analysis, 15 studies, in which 910 participants with HT underwent interventions of physical activity, which lasted 8 to 24 weeks of 3-5 sessions/week. Physical activity, mostly aerobic reduced 24-hour, daytime, and nighttime ambulatory blood pressure.<sup>25</sup> Somewhat differently a meta-analysis of 14 studies on 253 participants with HT found that the mean values of systolic and diastolic blood pressure decreased most significantly after strength training interventions.<sup>26</sup>

Wahid et al.<sup>27</sup> studying the relationships between physical activity and both cardiovascular disease and T2DM found that the greatest gain in health is associated with moving from inactivity to small amounts of physical activity, lending hope to intervention programs that seek to cause a change, even when minimal, as an initial encouragement to participants. Matos et al.<sup>28</sup> summarizing 6 studies, found that physical activity and exercise were effective non-pharmacological interventions to improve diabetic foot related outcomes. A large recent meta-analysis of 12 studies involving 3997 patients showed that diet and physical activity have a significant effect on blood glucose and weight control in patients with Type 2 diabetes mellitus.<sup>29</sup>

## Combination of diet and physical activity

Considering all the above, it is justifiable to administer a lifestyle modifying intervention as a holistic approach. An authoritative review by Valenzuela PL, et al.<sup>30</sup> concluded that major lifestyle interventions, such as regular physical exercise, body weight management and healthy dietary patterns, are the centerpiece of prevention and adjuvant treatment of hypertension. Accordingly, the American association of clinical endocrinology consensus statement algorithm of 2023 emphasizes lifestyle modification and treatment of overweight/obesity as key pillars in the management of prediabetes and diabetes mellitus.<sup>31</sup>

A finish study on 522 middle-aged, overweight people gave patients in the control group general oral and written information about diet (a two-page leaflet) and exercise at baseline and at subsequent annual visits, but no specific individualized programs were offered to them. They completed a three-day food diary at baseline and at each annual visit, using a booklet illustrating the sizes of portions of food. In contrast, people in the intervention group were given detailed advice about how to achieve the goals of the intervention, which were a reduction in weight of 5 percent or more, in total intake of fat to less than 30 percent of energy consumed, and in intake of saturated fat to less than 10 percent of energy consumed; an increase in fiber intake to at least 15 g per 1000 kcal; and moderate exercise for at least 30 minutes per day. Frequent ingestion of whole-grain products, vegetables, fruits, low-fat milk and meat products, soft margarines, and vegetable oils rich in monounsaturated fatty acids was recommended. The dietary advice was tailored to each person based on a three-day food record, completed four times per year. Each person in the intervention group had seven sessions with a nutritionist during the first year of the study and one session every three months thereafter. These people also received individual guidance on increasing their level of physical activity. Supervised, progressive, individually

tailored, circuit-type resistance-training sessions were also offered with the aim of improving the functional capacity and strength of the large muscle groups. Participants were instructed to perform a moderate-to-high number of repetitions and to take a break of 15 to 60 seconds between the stations on the circuit. During the first year, the rate of participation in these sessions varied from 50 percent to 85 percent at different centers. The net weight loss by the end of year 2 was  $3.5 \pm 5.5$  kg in the intervention group and  $0.8 \pm 4.4$  kg in the control group. The cumulative incidence of diabetes mellitus after four years was 11 percent in the intervention group and 23 percent in the control group (a 58% reduction).<sup>32</sup> All told, there is a meaningful advantage to intensive, personal involvement of medical personnel in driving a change of lifestyle.

A three-way study on 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations tested placebo, metformin (850 mg twice daily), or a lifestyle-modification program with the goals of at least a 7 percent weight loss and at least 150 minutes of physical activity per week. The average follow-up was 2.8 years. The incidence of diabetes was 11.0, 7.8, and 4.8 cases per 100 person-years in the placebo, metformin, and lifestyle groups, respectively. To prevent one case of diabetes during a period of three years, 7 people, compared to 14 with metformin, would have to participate in the lifestyle-intervention program. The same general insight on involvement of medical people was derived from this study as following the initiation of the program subsequent individual sessions (usually monthly) and group sessions with the case managers were designed to reinforce the behavioral changes. (Diabetes prevention program research group. 2002).

A meta-analysis of 27 studies explored the cost-effectiveness of lifestyle interventions and metformin in reducing subsequent incidence of Type 2 diabetes mellitus, both alone and in combination with a screening program to identify high-risk individuals. Intervention-only programs were in general more cost effective than programs that also included a

screening component. The longer the period evaluated, the more cost-effective interventions appeared. However, the exact mode of intervention varied significantly between studies.<sup>33</sup>

## What is the preferred mode of intervention for changing lifestyle

In general, one can see three modes of intervention for lifestyle modifying intervention. The first and minimal is the administration of information by paper, media or human lectures. The second is some form of tailored individual follow up by medical staff members to the participants, leaning on periodical reports and catching up on adherence. The third is initial guidance with the consequent formation of group meetings for the long run.

As mentioned above, some information and initial guidance were inferior to individual follow-up, protracted to a longer term. We haven't found in the available literature any specific recommendation as to the best time to initiate lifestyle modifying intervention. Yet, in the light of the key role of pregnancy and the birth of a new baby, it is reasonable to suggest an intervention as close to the event as feasible.

## The effect of added support group to lifestyle modifying intervention

Rosales CB, et al.<sup>34</sup> described the positive effect of an lifestyle modifying intervention program which included support group in the prevention of cardiovascular disease. Quansah DY, et al.<sup>35</sup> found that in 211 patients with GDM, the intervention for lifestyle modification which included support groups in the intervention group, yielded an increase in fat-free mass and less post-partum weight gain up to a year of follow up. van Dam HA, et al.<sup>36</sup> in a review found that compared to other interventions, only in the group consultations study, diabetes control was protected. To moderate the general scene Rejeski WJ, et al.<sup>37</sup> showed that lifestyle modifying intervention compared to support groups was better in improving the status of Type 2 diabetes mellitus obese patients.



Thus, one should conclude that the combination of the two is at least as good as lifestyle modifying intervention alone.

Chen & Li<sup>38</sup> who performed a meta-analysis of effectiveness of interventions using empowerment concept for patients with chronic disease found that group-directed interventions had more effect than individual-directed interventions on blood pressure in diabetic patients, thus reinforcing the notion of support group as an essential component in each LMI program. Chang MW, et al.<sup>39</sup> performed a study on 525 low-income overweight or obese women with young children, by introducing a designated video lesson at home and dialed in a peer support group teleconference every week (weeks 1-4) then every other week (weeks 5-16). They found that the intervention led to increased autonomous motivation, which subsequently increased self-efficacy, in turn associated with decreased dietary fat intake. They concluded that peer encouragement may be warranted in interventions to enhance autonomous motivation and/or practical skills for increasing self-efficacy. Likewise, Rosales CB, et al.<sup>34</sup> recruited 518 participants to a parallel, two-arm, cluster-randomized, behavioral clinical trial across 22 clinics in Sonora, Mexico, between August 2016 and October 2018. The program delivered a 13-week secondary prevention intervention, Meta Salud Diabetes, within the structure of a support group. They found that cardiovascular disease risk was lower for the intervention group, as was diabetes mellitus distress on the Meta Salud Diabetes arm.

## Conclusion

The current day's availability of ample food and lack of a need for physical activity in the industrialized nations led to increased rates of obesity HT and diabetes mellitus, decreasing health status and longevity. In women these pathologies reveal themselves earlier thanks to intercurrent pregnancies. This should lead to earlier lifestyle modifying intervention, aiming at dietary and physical activity profiles, of which those involving some form of support groups are the most promising.

Further research is needed to refine intervention strategies, define and address adherence challenges, integrate personalized and technology-driven approaches such as artificial intelligence, and inform policy changes that promote early screening and preventive care. These insights can aid healthcare providers and policymakers in optimizing clinical guidelines for metabolic health management in women.

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