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Maternal health and non-communicable disease prevention: An investment case for the post COVID-19 world and need for better health economic data

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Abstract

An integrated approach to population health, disease surveillance, and preventive care will dominate the health agenda in the post COVID-19 world. Because of their huge burden and the vulnerability imposed during a health crisis, prevention and care of non-communicable diseases (NCDs) will need to be prioritized even further. Maternal and child health are inextricably linked with NCDs and their risk factors. The intergenerational impact of poor maternal nutrition and health conditions during pregnancy, particularly NCD-related pregnancy complications, can be considered as a multiplier of the ongoing pandemic of NCDs. The economic cost of poor maternal health and NCD-related pregnancy complications is likely very high, but is not adequately researched or documented in the context of long-term population health. Interventions to address NCDs in pregnancy have beneficial effects on short-term pregnancy outcomes; but even more importantly, identifying "at-risk" mothers and offspring opens up the opportunity for targeted early preventive action. Preventive actions to address obesity, hypertension, type 2 diabetes, and cardiovascular diseases have a common lifestyle approach—identifying any one of these problems in pregnancy provides an opportunity to address them all. Cost–benefit analyses that only focus on the short-term and on one condition do not capture the full value of downstream, long-term benefits for population health. This requires urgent attention from FIGO.

KEYWORDS

COVID-19; Health economics; Health system transformation; Maternal health; NCD pregnancy complications; Non-communicable diseases

1 | INTRODUCTION

The ongoing coronavirus disease 2019 (COVID-19) pandemic is creating the biggest health, economic, and social crisis the world has confronted in living memory. When it ends it will leave behind bruised and battered health systems, economies, individuals and families, and society at large, across the world. The biggest impact, no doubt, will be on the economy and health systems and there will be a need to reassess priorities in health and how we access and deliver health care. Population health, disease surveillance, and preventive care will most likely dominate the agendas of international development agencies, as well as local, regional, and national governments.

Approximately 79% of people requiring intensive care in the USA[1] and 86% of deaths in New York State in the ongoing COVID-19 global pandemic,[2] as elsewhere around the world, have occurred in people with comorbid non-communicable diseases (NCDs) be it diabetes, hypertension, obesity, cardiovascular disease, a chronic respiratory condition, or cancer. While these deaths will be ascribed to COVID-19,

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the majority are the consequence of poor health due to the underlying comorbidity. NCDs are widely prevalent and, even in normal times, directly or indirectly account for most deaths (often premature) worldwide. In the post COVID-19 world, prevention and care of NCDs will have to be prioritized even further to improve population health; and what better place to begin than when life begins.

2 | MATERNAL OFFSPRING HEALTH AND FUTURE NCDS

Maternal and child health is inextricably linked with NCDs and their risk factors. Specifically, conditions such as prenatal malnutrition and low birth weight create a predisposition to obesity, type 2 diabetes, hypertension, and heart disease later in life. Furthermore, maternal overweight and obesity, gestational hypertension and pre-eclampsia, and gestational diabetes are associated with a higher risk for the above conditions in both the mother and offspring.

Poor maternal nutrition and health during pregnancy may be considered as a multiplier of the ongoing pandemic of NCDs, particularly in low-resource countries, since it provides a crossover bridge for undernutrition in one generation to transit to overweight and obesity in the next generation through gestational hyperglycemia and macrosomia; thereby impacting subsequent generations with overweight, obesity, type 2 diabetes, and cardiovascular diseases among others.[3] Poor maternal health increases the risk of NCDs in the offspring, and in subsequent generations NCDs lead to poor maternal health, setting a vicious cycle of intergenerational risk transmission through developmental programming.[4]

Of the approximately 130 million pregnancies resulting in live births globally every year, an estimated 21 million are impacted by hyperglycemia, about 7–8 million by hypertension, about 42 million by maternal overweight and obesity, 26 million by maternal undernutrition, and 56 million by maternal anemia.[5] Not only do these conditions increase the risk of adverse pregnancy outcomes and increase perinatal morbidity and mortality, but they also identify both the mother and the offspring at high risk for future diabetes, obesity, hypertension, cardiovascular disease, and stroke.

Medical conditions that are exacerbated by pregnancy, such as obesity, diabetes, cardiovascular disease, among others, already account for over 28% of maternal deaths worldwide,[6] with the number only likely to increase further over time. They also impact fetal growth (intrauterine growth restriction, small for gestational age, macrosomia and large for gestational age) and increase the risks of prematurity, stillbirth, congenital malformations, birth injuries, respiratory distress, and hypoglycemia, among others, at birth. The economic cost of NCD-related pregnancy complications is likely very high, but is unfortunately not adequately researched nor documented.

Overweight and obesity in pregnancy not only cause problems of their own but also increase the risk of hyperglycemia, hypertension, and pre-eclampsia. Similarly, hyperglycemia in pregnancy increases the risk of hypertension and pre-eclampsia, thereby compounding adverse pregnancy outcomes. While there are studies addressing the costs of individual NCDs, their combined impact associated with causing pregnancy complications and compounding costs has rarely been studied, despite the clear interconnectedness.

The presence of these conditions during pregnancy is a reliable marker for future NCDs in both the mother and offspring. Thus, overweight or obese pregnant women without gestational diabetes or gestational hypertension continue to be at high risk for future type 2 diabetes, hypertension, and cardiovascular disease later in life. Similarly, women with gestational diabetes, apart from being at very high risk of type 2 diabetes, are at high risk of future hypertension and cardiovascular disease, as are women with gestational hypertension and pre-eclampsia. In addition, the offspring of pregnancies impacted by any of these NCDs are also at risk of obesity and cardiometabolic problems.

Interventions to address NCDs in pregnancy have beneficial effects on the short-term pregnancy outcomes. Whether treatment during pregnancy will prevent or reduce long-term maternal and offspring risks is currently unknown and requires further well-designed, long-term intervention studies. Nonetheless, identifying "at risk" mothers and offspring opens up the opportunity for targeted early preventive action, which has been shown to be beneficial for some conditions such as gestational diabetes (described later). Since preventive actions to address obesity, hypertension, type 2 diabetes, and cardiovascular diseases have a common lifestyle approach, identifying any one of these problems in pregnancy provides an opportunity to address them all. Cost–benefit analyses that only focus on the short term and one condition do not capture the full value of downstream, long-term benefits for population health.

3 | HYPERGLYCEMIA IN PREGNANCY

Hyperglycemia is now one of the most common medical conditions seen during pregnancy. The International Diabetes Federation (IDF) estimates that 21 million live births (1 in 6 or 16.8%) occur in women with some form of hyperglycemia in pregnancy (HIP), of which 2.5% may be due to overt diabetes in pregnancy.[7] The other 14.3% (1 in 7 pregnancies) is due to gestational diabetes mellitus (GDM), a condition that may reflect pre-existing prediabetes or develop due to hormonal changes of pregnancy and is confined to the duration of pregnancy.[7]

HIP significantly increases the risk of pregnancy complications such as hypertension, pre-eclampsia, stillbirth, premature delivery, both large- and small-for-gestational-age babies, obstructed labor, postpartum hemorrhage, infections, birth injuries, congenital anomalies, and newborn deaths due to respiratory problems, hypoglycemia, etc. Available evidence shows that HIP is associated with a high risk of maternal and perinatal morbidity and mortality and poor pregnancy outcome.[8–10] It has also been shown that women with a history of GDM are at a high risk of future diabetes and cardiovascular disease.[11–13] Offering these women postpartum lifestyle intervention and treatment prevents or delays the onset of diabetes and cardiovascular disease,[14–16] thus providing a unique opportunity for primary prevention of these conditions. In addition, the offspring of

GDM pregnancies are at high risk of metabolic problems[17,18] including early onset type 2 diabetes.[19] Treatment of maternal diabetes is expected to reduce these risks; however, there is still limited evidence from high-quality studies.[20,21]

3.1 | Health economics

There are only a few studies that have evaluated the cost-effectiveness of an integrated approach to GDM screening and care that also include the postpartum prevention component. Most studies have evaluated the cost-effectiveness of one screening strategy over another; for example, selective screening versus universal screening, or the International Association of Diabetes in Pregnancy Study Groups (IADPSG) criteria over the World Health Organization (WHO) 2009 criteria or the American Diabetes Association (ADA)/American College of Obstetrics and Gynecology (ACOG) criteria.

Using a decision analysis tool, GeDiForCE (Gestational Diabetes Formulas for Cost-Effectiveness, developed by UCSF and Health Strategies International with funding from Novo Nordisk A/S), which assesses the full range of costs and benefits of GDM screening and intervention in specified populations, Marseille et al.[22] reported that the intervention is highly cost-effective in India and Israel. The program cost in international dollars per 1000 pregnant women was $259 139 in India and $259 929 in Israel. Net costs, adjusted for averted disease, were $194 358 and $76 102 in India and Israel, respectively. The costs per disability-adjusted life years (DALY) averted were $1626 in India and $1830 in Israel.

A decision analysis modelling study from the USA by Werner et al.[23] compared the cost–utility of three strategies to identify GDM: (1) no screening; (2) current screening practice (1-hour 50-g glucose challenge test between 24 and 28 weeks followed by 3-hour 100-g glucose tolerance test when indicated); or (3) screening practice proposed by IADPSG. The primary outcome measure was the incremental cost-effectiveness ratio (ICER). For every 100 000 women screened, 6178 quality-adjusted life years (QALYs) are gained, at a cost of US $125 633 826. The ICER for the IADPSG strategy compared with the current standard was US $20 336 per QALY gained. When post-delivery care was not accomplished, the IADPSG strategy was no longer cost-effective.

Mission et al.[24] used a decision analysis model to compare the cost-effectiveness of treating patients with GDM versus not treating in the USA. They considered patients in HAPO (Hyperglycemia and Adverse Pregnancy Outcome) Category 5 (top 3%–12% of fasting glucose levels), which is consistent with diagnosis of marginal patients according to the IADPSG recommendations. Treating patients was found to be cost-effective at a cost of US $44 203 per QALY. A one-way sensitivity analysis suggested that treatment remained cost-effective when it met 64% of its reported efficacy. Ohno et al.[25] compared treating versus not treating mild gestational diabetes from a societal perspective. In the base-case analysis, treatment was found to be cost-effective at US $20 412 per QALY below willingness to pay (WTP) threshold of US $100 000.

An Australian study by Moss et al.[26] compared treatment of women with mild gestational diabetes by dietary advice, blood glucose monitoring, and insulin therapy as needed with routine pregnancy care from a health system perspective. Based on data from the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) trial, the incremental cost per additional serious perinatal complication (defined as one or more of the following: death, shoulder dystocia, bone fracture, nerve palsy) prevented, was estimated at AU $27 503. The incremental cost per perinatal death prevented was calculated as AU $60 506 and AU $2988 per life-year saved.

A study from China using the GeDiForCE model assessed the cost-effectiveness of GDM screening versus no GDM screening.[27] The total costs of GDM screening, intervention, and life-time preventive care per 1000 pregnant women was international dollars $7 092 398 in the GDM screening group, saving $1 329 671 in costs compared with the no screening group. A total of 277 DALYs were averted in the screening group, mainly as a consequence of postpartum care for type 2 diabetes prevention. Sensitivity analyses demonstrated robustness of the results.

Another study from China reported that the average cost of a pregnancy with GDM in China in 2015 was CNY ¥6677.37 (international $1929.87), which was 95% higher compared with a pregnancy without GDM due to additional expenses both during pregnancy and at delivery (CNY ¥4421.49 for GDM diagnosis and treatment; CNY ¥1340.94 (+26%) for maternal complications; and CNY ¥914.94 (+52%) for neonatal complications.[28] In China, 16.5 million babies were born in 2015 with a GDM prevalence rate of 17.5%—an estimated 2.90 million pregnancies in 2015 were affected by GDM. Therefore, the annual direct short-term cost due to GDM was estimated to be CNY ¥19.36 billion (international $5.59 billion).[28]

The estimation of the direct health and economic burden of maternal overweight, GDM, and related macrosomia indicates that associated healthcare expenditures are substantial. The calculation of a budgetary impact of GDM, based on a conservative approach, using USA costing data in the model, indicates an annual cost of more than US $1.8 billion without considering long-term consequences.[29]

Another US study reported that each case of GDM is associated with US $5800 in higher medical expenditures.[30] The overall health and economic costs associated with unrecognized and untreated GDM will undoubtedly be several fold higher, underscoring the importance of screening for and management of GDM.

A study to evaluate the preventable health and cost burden of adverse birth outcomes associated with pregestational diabetes (PGDM) in the USA reported that universal preconception care might avert 8397 (90% prediction interval [PI], 5252–11 449) preterm deliveries, 3725 (90% PI, 3259–4126) birth defects, and 1872 (90% PI, 1239–2415) perinatal deaths annually.[31] Associated discounted lifetime costs averted for the affected cohort of children could be as high as US $4.3 billion (90% PI, 3.4–5.1 billion) (2012 US dollars). Preconception care (including screening for diabetes) among women with undiagnosed diabetes could yield an additional US $1.2 billion (90% PI, 951 million–1.4 billion) in averted cost.[31]

Evidence from prospective studies demonstrates that lifestyle and pharmacological interventions for prevention of diabetes are as effective in women with GDM as in non-GDM women with impaired glucose tolerance (IGT) and men with IGT.[14–16] A recent study showed

that not only does metformin treatment continue to exert its diabetes prevention effect 15 years after randomization in the Diabetes Prevention Program (DPP) and the Diabetes Prevention Program Outcomes Study (DPPOS), but its effect was also significantly better in women with a history of prior GDM compared with parous women with IGT without previous GDM.[32]

Breast feeding for more than 10 months has also been reported to decrease the risk of diabetes mellitus 2 years after delivery by 57% in women with a history of GDM.[33]

Given that lifestyle interventions or use of medications for prevention of diabetes in people at risk in various settings are regarded as highly cost-effective and that treatment of GDM is cost-effective in preventing perinatal complications, it seems intuitive that screening and comprehensive care for GDM should be highly cost-effective overall, even in the absence of more cost-effectiveness data.[29]

4 | OVERWEIGHT AND OBESITY

Complications of overweight and obesity during pregnancy include hypertensive disorders, coagulopathies, GDM, respiratory problems, and fetal complications such as large-for-gestational-age babies, congenital malformations, stillbirth, and shoulder dystocia. Risk of pre-eclampsia increases 2–3-fold in women overweight in early pregnancy.[34] Obesity is associated with an increased risk of maternal infection (adjusted odds ratio [aOR] 3.35)[35]; cesarean delivery (aOR 3.50)[35]; prolonged hospital stay (aOR 2.84)[35]; pre-eclampsia (aOR 4.46)[36]; induction of labor (aOR 1.97)[36]; postpartum hemorrhage (aOR 3.04)[36]; maternal intensive care admission (aOR 3.86)[36]; GDM (aOR 7.89)[36]; thrombosis (aOR infinity)[36]; shoulder dystocia (aOR 1.89)[36]; and instrument-assisted delivery (aOR 1.17).[36]

Maternal overweight and obesity (body mass index [BMI] greater than 25, calculated as weight in kilograms divided by the square of height in meters) is the most important modifiable risk factor for stillbirths in high-income countries, contributing to around 8000 stillbirths (22 weeks of gestation) annually.[37] In low-income countries, apart from stillbirths, complications relate to the 2–3-fold increased risk of macrosomia, requiring institutional and assisted delivery. When these services are not available, significantly higher maternal morbidity and mortality may ensue.[38]

4.1 | Health economics

Very few studies have assessed the economic costs of overweight and obesity associated with pregnancy. It has been estimated that the total costs for overweight and obese pregnant women with GDM during pregnancy and up to 2 months following delivery increase by 23% and 37%, respectively, compared with women with normal BMI.[39,40] Infant healthcare usage cost is also linked to maternal BMI. Total mean additional cost, in a study from within the National Health Service in the UK, was estimated at £65.13 for infants born to overweight mothers and £1138.11 for infants born to obese mothers, when compared with infants of healthy weight mothers.[41]

5 | HYPERTENSION AND PRE-ECLAMPSIA

Hypertension is a significant contributor to pregnancy-related complications. It can occur as gestational hypertension, pre-eclampsia, chronic hypertension, or pre-eclampsia superimposed on chronic hypertension. Although the incidence varies in different parts of the world, overall, nearly 10% of normotensive women experience abnormally elevated blood pressure at some point during pregnancy. Hypertensive disorders of pregnancy (HDP) complicate 5%–10% of pregnancies and are increasing with the rising prevalence of overweight, obesity, diabetes, and metabolic disorders in younger, women of reproductive age.[42]

Worldwide, high blood pressure with or without proteinuria is a major cause of maternal morbidity and mortality[43] and HPDs account for 10%–15% of maternal deaths in low- and middle-income countries,[44–46] as well as to increased perinatal morbidity and mortality as a consequence of prematurity and poor fetal growth. Pre-eclampsia typically affects 2%–5% of pregnant women and is one of the leading causes of maternal and perinatal morbidity and mortality, especially when the condition is early onset[47,48]; globally, 76 000 women and 500 000 babies die each year from this disorder.[49] Furthermore, women in low-income countries are at a higher risk of developing pre-eclampsia compared with those in high-income countries.[50]

Women who develop gestational hypertension and pre-eclampsia have a greater chance of developing cardiovascular disease and type 2 diabetes in later life.[51] Despite this, they do not routinely receive long-term follow-up,[52] counseling, or risk factor stratification and evaluation.

Compared with an uncomplicated pregnancy, costs associated with pre-eclampsia are significantly higher, for both the mother and the neonate, in any given regional setting. This is because of its severity and life-threatening nature requiring advanced intensive care. The cost of an uncomplicated vaginal delivery in California in 2011 was estimated to be about US $4500[53] and the average incremental cost of a pregnancy complicated by hypertensive disease was estimated to be US $8200; amounting to an additional cost of US $200 million for all Californian births. Costs were highest for women who had severe disease requiring early delivery (<34 weeks). In this particular cohort, the incremental cost was US $70 100 per pregnancy.[53]

In Ireland, although the costs of an uncomplicated delivery are lower (US $3000) compared with California, the cost escalation for pregnancies affected by pre-eclampsia was similar (increment of US $3300)[54]; the predominant cost escalator was neonatal care for preterm birth.[55] Whereas costs of maternal care increased 2.7-fold for women delivering before 32 weeks, costs of neonatal care increased 35-fold.

The annual financial burden of pre-eclampsia in the USA in 2012, including the care of mother and child for the first 12 months after delivery, was US $2.18 billion; US $1.03 billion for mothers and US $1.15 billion for infants. The cost burden per infant is dependent on

gestational age, ranging from US $150 000 at 26 weeks to US $1311 at 36 weeks.[56]

Use of low-dose aspirin to prevent pre-eclampsia in women at risk is well accepted and the ASPRE trial conclusively proved its value in preventing preterm pre-eclampsia.[57] The findings have implications for both short- and long-term healthcare costs as well as infant survival and handicap.[58]

5.1 | Health economics

Using a decision analysis model, the clinical and economic benefits of a first-trimester screening program based on the Fetal Medicine Foundation algorithm for prediction of early-onset pre-eclampsia coupled with early (<16 weeks) use of low-dose aspirin in those at high risk was simulated and tested with current practice in Canada.[59] Among the theoretical 387 516 births per year in Canada, the estimated prevalence of early pre-eclampsia based on first-trimester screening and aspirin use declined 1.5-fold to 705 cases compared with 1801 cases based on current practice. This resulted in an estimated saving of C $13 130 per case averted (C $14.39 million annually).[59] Other studies show similar findings.[60–64]

These recent studies should also be compared with the findings of the 2008 National Institute for Health Research Health Technology Assessment (HTA), which published a detailed consideration of the evidence relating to screening for pre-eclampsia.[65] Unlike other modelling exercises, it systematically considered all possible tests and management interventions available at that time in a variety of different strategies rather than a single one. In particular, it considered strategies in which treatments were applied without any previous testing ("No test/treat all"). The results led to the conclusion that the most cost-effective approach to reducing pre-eclampsia was the provision of an effective, affordable, and safe intervention (such as low-dose aspirin) applied to all mothers without previous testing.

However, if the long-term implications of pre-eclampsia such as future risk of cardiovascular disease and type 2 diabetes are taken into account, the "No test/treat all" strategy will be inferior as it would fail to identify women at risk for future cardiometabolic problems and could benefit from intensive postpartum follow-up and lifestyle interventions.

6 | CHALLENGES AND OPPORTUNITIES IN ADDRESSING NCD-RELATED PREGNANCY COMPLICATIONS

From a large-scale program perspective, there are two key challenges in effectively improving pregnancy outcomes, particularly in low- and low/middle-income countries. First is the inability of health systems to screen women for common medical conditions that create pregnancy complications early enough (preconception, first trimester), to identify women requiring treatment and preventive care. The second is the inability to track and follow up women with an NCD-related pregnancy complication after delivery to continuously engage and empower the at-risk mother-child pair to adopt a healthy lifestyle.[66] Without adequate focus on postpartum care, the strategy for screening and treatment of common NCDs during pregnancy is only half as effective. Focusing only on the short-term survival in terms of lowered maternal and perinatal morbidity and mortality does not capture outcomes that have longer-term implications for adult health, life expectancy, quality of life, and accumulation of human capital.[67] 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 intergenerational prevention of several chronic diseases.[68] Multiple barriers stand in the way of these objectives. The barriers related to GDM, for example, have been described in a systematic review[69] and efforts should be made to mitigate these barriers to achieve program objectives.

A 2007 publication by Abegunde et al.[70] noted that the estimated age-standardized death rate from chronic diseases in 23 low-income and middle-income countries with 80% of the global NCD burden was higher (54%) for men and even higher (86%) for women compared with those in high-income countries.

In 2014, Stenberg et al.[71] described how investment in women's and children's health will secure high health, social, and economic returns. Increasing health expenditure by just US $5 per person per year up to 2035 in 74 high-burden countries could yield up to nine times its value in economic and social benefits. These returns include greater gross domestic product growth through improved productivity, and prevention of the needless deaths of 147 million children, 32 million stillbirths, and 5 million women by 2035. These gains could be achieved by an additional investment of US $30 billion per year, equivalent to a 2% increase above current spending.

In 2018, Bertram et al.[72] noted that an additional investment of US $1.50 per capita per year would avert 15 million deaths, 8 million incidents of ischemic heart disease, and 13 million incidents of stroke in the select 20 countries studied. Benefit–cost showed a ratio of 5.6 for economic returns but the ratio increased to 10.9 when social returns are included. Investing in NCD prevention is integral to achieving Sustainable Development Goal (SDG) target 3.4 (reducing premature mortality from NCDs by a third) and to progress toward SDG target 3.8 (the realization of universal health coverage).

Despite the clear logic and some health economic evidence, why is it that the link between maternal health and prevention of NCD is continually neglected? Perhaps the silo approach to health that divides healthcare delivery into communicable and non-communicable diseases and maternal and child health is partly responsible. This division extends even within maternal child care, such that long-term postpartum follow-up of women with demonstrated pregnancy complications is not linked to the child's follow-up and vaccination program, which provides an opportunity to track the high-risk mother–child pair. The other reason is perhaps that the health economic impact of addressing overall maternal health is addressed merely in terms of the short-term outcomes of different conditions and not in the integrated longer-term impact on future population health when combined with continued tracking, engaging, and empowering for healthy lifestyles.[66]

As the global voice for women's health, FIGO needs to give urgent attention to this area, in particular creating health economic evidence for an integrated approach to maternal health and NCD prevention. When health system priorities are reconfigured in the post-COVID-19 world, the "silo mentality" will have to be broken down to transform health systems. What better place to begin the transformation than where life begins, ensuring the health of women before, during, and after pregnancy and of their offspring in a life course approach that is not merely theoretical but pragmatic and economical to society—an approach that documents, tracks, empowers, and proactively engages reproductive-age people and their offspring for good health.

AUTHOR CONTRIBUTIONS

AK wrote the first draft, which was reviewed and commented by MH. Both authors contributed to the final article.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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