Gestational Diabetes Mellitus: a Growing Economic Concern

Radiana Staynova¹, Emanuela Vasileva²,⁴, Vesselina Yanachkova³

¹ Department of Pharmaceutical Sciences, Faculty of Pharmacy, Medical University of Plovdiv, Plovdiv, Bulgaria
² Department of Propaedeutics of Internal Diseases, Faculty of Medicine, Medical University of Plovdiv, Plovdiv, Bulgaria
³ Dr Shterev Hospital, Sofia, Bulgaria
⁴ Clinic of Endocrinology and Metabolic Disorders, Kaspa University Hospital, Plovdiv, Bulgaria

Corresponding author: Radiana Staynova, Department of Pharmaceutical Sciences, Faculty of Pharmacy, Medical University of Plovdiv, 15A Vassil Aprilov, 4002 Plovdiv, Bulgaria; Email: radiana.staynova@mu-plovdiv.bg; Tel.: +359 32/200 768

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Abstract

Gestational diabetes mellitus (GDM) is a common pregnancy complication. Recent epidemiological data have shown that GDM prevalence has been on the increase worldwide. GDM could lead to adverse pregnancy outcomes and is usually associated with higher costs for its treatment and management. Pharmacoeconomics has become a crucial component of the healthcare systems in recent years because of the steadily rising costs. Despite this, there are few pharmacoeconomic studies evaluating the expenses of pregnancies impacted by GDM. This article presents a brief introduction to pharmacoeconomics and provides awareness of the economic impact of GDM. Studies associated with health care costs of GDM were reviewed and an attempt was made to determine its global economic burden.

Keywords

gestational diabetes, pharmacoeconomics, costs

INTRODUCTION

In their reproductive years, women use health services to a greater extent than men do.¹,² The reason for this discrepancy is the health expenditures women have for medical care during pregnancy and childbirth, and the treatment of prenatal complications.¹ In general, medical expenditures of pregnant women include the costs for antenatal care during pregnancy, inpatients visits, delivery, and newborn baby’s care.² Pregnancy could be followed by numerous complications that contribute to considerably higher costs.²,³ In addition to health care costs, there are indirect costs that can occur during pregnancy – like unexpected absences from work or short- and long-term disability.

Gestational diabetes mellitus (GDM) is a common pregnancy complication. It is associated with short- and long-term consequences for both mother and child, including obesity, metabolic syndrome, and the development of type 2 diabetes mellitus (T2DM) later in life. Early diagnosis and adequate therapeutic intervention can significantly improve pregnancy outcome and long-term consequences for women with this condition and their children.⁴ In addition, GDM is associated with higher costs for treatment and management.²

An important goal in GDM management is to maintain blood glucose levels close to the normal level for pregnancy.⁵ This can be achieved through lifestyle modification and/or insulin therapy combined with regular self-monitoring of blood glucose.² Outpatient treatment of GDM is the preferred strategy due to the societal and financial benefits it provides. Nevertheless, in some cases short-term hospitalizations are required, which are associated with additional costs.²,⁶
GDM affects a woman’s health for a very short period but could have long-lasting adverse effects at significantly high monetary, humanitarian, and social costs. Pharmacoconomics has become an integral part of the healthcare system in recent years as a result of the steadily rising expenditures. Despite this, there are very few pharmacoeconomic studies evaluating the expenses of pregnancies affected by GDM.

A pharmacoeconomic analysis of GDM aims to assist financial institutions and decision-makers in estimating the amount of money required to treat and manage these pregnancy complications.

**Significance of pharmacoeconomic assessment**

In the 21st century, the traditional role of health care providers has changed dramatically, as evidenced by the growing importance and participation of Pharmacoconomics as a scientific discipline. The accelerated rise of prescribing and dispensing costs, coupled with continued increases in the expenditure on drugs and medical devices, puts pharmacoeconomics at the forefront of optimal drug therapy.

Although relatively young, this field of knowledge is of particular importance in the modern world, since it adopts and applies the principles and methodology of health economics in the field of drug policy. The term “pharmacoeconomics” was first mentioned in 1986, during the annual meeting of pharmacists in Toronto, Canada, where Ray Townsend of the pharmaceutical company Upjohn used the term in his presentation. Townsend defines pharmacoeconomics as “a description and analysis of the costs of drug therapy for health care systems and society.”

Pharmacoeconomics applies economic analysis to the use of medicines, health care services and programs, focusing on the costs and outcomes of this use. The results are related to the measurement of health, economic, and social outcomes of drug use.

Economic research in health care is becoming increasingly necessary as it allows to objectively assess all costs associated with the treatment of diseases, as well as to compare alternative methods and approaches offered by a variety of medicines and treatment regimens.

Pharmacoeconomics finds wide practical application in the pricing of medicinal products, drug and reimbursement policy, marketing of pharmaceutics, clinical trials, post-marketing studies, etc. The two main components of a pharmacoeconomic evaluation are cost and outcomes. Every resource used in health care means that there are costs associated with it. Proper identification and measurement of costs are crucial for accurate evaluation.

Costs could be categorized into four groups: direct medical costs, direct non-medical costs, indirect costs, and intangible costs. Drummond et al. offer an alternative way of classifying costs according to their place of origin. According to this criterion, the costs are divided into four categories: health care system costs, costs to other sectors, patient and family costs, and costs related to loss of productivity.

The inclusion of different cost categories in pharmacoeconomic studies, where possible, provides a more accurate assessment of the overall economic impact of the health program or treatment alternatives on a specific population or patient.

In pharmacoeconomics, regarding how health outcomes are measured and compared, four types of studies are used: cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA).

The choice of perspective is a guiding principle in performing a pharmacoeconomic analysis. It determines the choice of analysis as well as which of the costs and outcomes should be included in the evaluation.

GDM is a problem with social and economic consequences. It is found that this condition is a costly disease not only for the pregnant woman and her family, but for the society and health care systems as well. Women with GDM are a risk group that requires higher use of health care services. This justifies the importance of conducting pharmacoeconomic studies. These studies should answer the question whether the additional cost of treatment leads to changes in the quality of life, and whether there are any additional benefits from treatment related to the prevention of late complications both for the mother and the fetus.

A major difficulty for the health care systems is the ability to track and follow up the women with previous GDM and their children. There should be more pharmacoeconomic studies on women with previous GDM that focus on the different alternatives for managing the risk factors and lowering health care expenditures by preventing T2DM.

Pharmacoeconomic studies up to date give researchers the opportunity of analyzing expenditure linked to future prophylaxis of complications in women with a history of GDM. All these challenges unsolved cause the pharmacoeconomics importance and significance in the field of GDM.

**Costs attributed to GDM**

GDM-related costs could be categorized into three types: direct costs (medical and non-medical), indirect costs, and intangible costs (Fig. 1).

**Direct cost associated with GDM**

These costs are directly related to the diagnosis, treatment, delivery and prevention of complications. Direct medical costs include the medically related expenditures used to provide the treatment or prevention.
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Figure 1. Examples of GDM-related costs.

Direct non-medical cost associated with GDM

These are costs to the pregnant woman and her family that are directly related to the treatment of GDM, but are not medical in nature. Examples of non-medical costs include: travel costs to and from the healthcare facility, costs of hiring a babysitter, special diet costs, etc.

Indirect costs

Indirect costs include costs that occur from the loss of productivity because of illness. Examples of these costs are the value of productive time lost due to GDM, mother’s absence from work, reduced productivity while at work, partner’s (family member) time off work, etc.

Intangible costs

GDM could have a negative impact on the health-related quality of life of pregnant women. Intangible costs involve the costs related to pain, suffering, psychological stress, depression, fatigue or anxiety that result from the disease or its treatment. These costs are very difficult to measure.

Cost-effectiveness of GDM screening including prevention of T2DM

The majority of the pharmacoeconomic studies related to GDM assess the cost-effectiveness and benefits of screening programs. The conclusion most studies reach is that universal screening for GDM is a cost-effective strategy.

In most countries worldwide, a selective screening based on risk factors for GDM is preferred. Some of the risk factors include maternal age, overweight and obesity (BMI > 30 kg/m²), ethnicity, family history of diabetes, previous GDM, polycystic ovary syndrome, and previous macrosomia. However, focusing only on the risk factor-based approach, half of the women with GDM will not be correctly identified.

The International Federation of Gynecology and Obstetrics (FIGO) recommends the universal screening which is particularly relevant to low-, low-middle, and middle-income countries, where 90% of all cases of GDM are found and ascertainment of risk factors is poor owing to low levels of education and awareness, and poor record keeping. Only in this way, real savings will be provided, which could be used in the treatment of long-term maternal and neonatal complications in women with late-onset or undiagnosed GDM.
Weile et al. [24] reviewed cost-effectiveness research of GDM screening and analyzed its potential impact on global health. The researchers found that cost-effectiveness ratios varied widely due to geographic differences, diagnostic criteria, and outcomes. Most studies included in the review focused on the costs of screening itself, leaving eventual long-term saved costs unidentified. The authors recommended that decision-makers should focus on national or regional instead of global conditions. This would incorporate the potential of preventing effects on T2DM and other long-term complications for both mothers and their children. [24]

The recent systematic review conducted by Werbrouck et al. explored the literature on cost-effectiveness studies of screening and prevention of T2DM in women with previous GDM. The researchers summarized that an oral glucose tolerance test (OGTT) per three years leads to the lowest cost per case detected, and prevention is potentially cost-effective or cost-saving. [25]

**Short-term cost of GDM**

Most of the studies estimating the economic burden of GDM only account for short-term direct (medical and non-medical) and indirect costs. [26-32] Table 1 presents a summary of some of these studies.

A recent study[26] estimated the short-term costs of GDM in Mexico. A decision analytic model was built to compare the incremental costs of GDM-pregnancy and normal pregnancy. Cost evaluation includes the costs related to screening, follow-up, self-monitoring, pharmacological treatment, and delivery care. The cost of a pregnancy complicated by GDM was $2934.9 and the total additional cost was $1576.2 per case. Considering the substantial variability of the GDM incidence in Mexico, the authors reported that the total burden could range from $86.8 to $827.4 million per year. [26]

Data from the research conducted by Lenoir-Wijnkoop et al. [27] show that hyperglycemia during pregnancy was

**Table 1. Summary of selected studies accessing short-term economic burden of GDM**

<table>
<thead>
<tr>
<th>Study, year</th>
<th>Country</th>
<th>Study design</th>
<th>Study duration</th>
<th>Perspective</th>
<th>Currency/Price year</th>
<th>Cost category included</th>
<th>Mean difference in healthcare costs between a normal pregnancy and GDM-pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sosa-Rubi et al., 2019[26]</td>
<td>Mexico</td>
<td>Modeling</td>
<td>From the first trimester until childbirth</td>
<td>Health care system</td>
<td>US dollars, 2017</td>
<td>Direct medical costs</td>
<td>$1576.2</td>
</tr>
<tr>
<td>Meregaglia et al., 2018[30]</td>
<td>Italy</td>
<td>Modeling</td>
<td>3 months (from the 28th gestational week until childbirth)</td>
<td>Health care system</td>
<td>Euro, 2014</td>
<td>Direct medical costs</td>
<td>€817.8</td>
</tr>
<tr>
<td>Xu et al., 2015[29]</td>
<td>China</td>
<td>Modeling</td>
<td>3 months (last trimester of pregnancy)</td>
<td>Health care system</td>
<td>Chinese Yuan, 2015</td>
<td>Direct medical costs and health loss</td>
<td>¥6677.37 ($1929.87)</td>
</tr>
<tr>
<td>Lenoir-Wijnkoop et al., 2015[27]</td>
<td>USA</td>
<td>Modeling</td>
<td>From the first trimester until childbirth</td>
<td>Health care system</td>
<td>US dollars, 2014</td>
<td>Direct medical costs</td>
<td>$15593</td>
</tr>
<tr>
<td>Law et al., 2015[28]</td>
<td>USA</td>
<td>Retrospective comparative cohort study</td>
<td>During pregnancy and 3 months postpartum</td>
<td>Health care system</td>
<td>US dollars, 2011</td>
<td>Direct medical costs</td>
<td>$4560</td>
</tr>
<tr>
<td>Kolu et al., 2012[31]</td>
<td>Finland</td>
<td>Based on CRT †</td>
<td>From the beginning of the pregnancy until hospital discharge</td>
<td>Societal and patient</td>
<td>Euro, 2009</td>
<td>Direct medical costs</td>
<td>€1289</td>
</tr>
<tr>
<td>Moss et al., 2007[32]</td>
<td>Australia</td>
<td>Based on RCT ‡</td>
<td>9 months</td>
<td>Health care system and patient</td>
<td>AU dollars, 2002</td>
<td>Direct (medical and non-medical) and indirect costs</td>
<td>$A650 ($462.02)</td>
</tr>
</tbody>
</table>

† CRT: cluster-randomised trial; ‡ RCT: randomised control trial
associated with an average additional cost of $15,593 per pregnant woman, which consisted mainly of the cost of treating maternal complications ($11,794) and the cost of neonatal complications associated with fetal macrosomia ($3,799). The authors reported an annual budget impact of GDM for the United States of more than $1.8 billion.[27]

The results of another study from the United States also show that diabetes during pregnancy cost an additional $4,560 compared to non-diabetic pregnancies, which is a 30% increase.[28]

A recent study from China[29] analyzed the health and economic burden of GDM by estimating short-term costs. The average cost of pregnancy with GDM was ¥6677.37 ($1929.87 million in 2015) more than a pregnancy without GDM due to the additional costs during both pregnancy and childbirth. With GDM prevalence of 17.5% in China, the number of pregnant women affected by GDM was 2.90 million in 2015. The annual socio-economic burden of the GDM was estimated at ¥19.36 billion ($5.59 billion). The total incremental health losses associated with GDM were estimated at approximately 260.000 quality-adjusted life years (QALYs). The researchers assumed that GDM had a significant economic impact on the health care system. Their findings show a clear need to implement strategies for the prevention and treatment of GDM as well as rise public awareness.[29]

A similar study was conducted in Italy.[30] Outpatient costs were estimated at €43.7 in normal pregnancies, compared to €370.6 in pregnancies affected by GDM (including costs for specialist consultations, laboratory tests, examinations, insulin therapy, medical devices and consumables). The costs for hospitalization were €1649.8 and €1150.3 for women with normal pregnancies and their children, and €1702.0 and €1407.7 for women with GDM and their children, respectively. Each pregnancy complicated by the GDM cost 22.4% more than a normal one, which corresponded to €636.5 per case. With a prevalence rate of 10.9%, the number of pregnancies affected by the GDM was estimated at 54,783 (out of 502,596 births) in 2014, leading to an additional cost of around €34.9 million for the national healthcare system. The loss in utility to mothers alone was estimated at about 5000 QALYs.[30]

Similar studies[31,32] have also been conducted in Australia and Finland. The authors reported that the average difference in health care costs between women with normal pregnancies and those diagnosed with GDM was about $462.02 and €1,289, respectively.[31,32]

**Costs and benefits of GDM treatment**

Using a decision analytic model, Ohno et al.[33] compared treating with not treating mild GDM. The results showed that treating mild GDM was cost-effective in terms of improving maternal and neonatal outcomes including decreased rates of preeclampsia, cesarean sections, macrosomia, shoulder dystocia, permanent and transient brachial plexus injury, neonatal hypoglycemia, neonatal hyperbilirubinemia, and neonatal intensive care unit admissions.[33]

Researchers from Brazil[2] estimated the cost-benefit relationship of hospitalization, compared with outpatient care, for pregnant women with GDM. The results from the study showed that successful treatment avoided expenditure of $1517.97 and $1127.43 for patients treated with inpatient and outpatient care, respectively. Conducted cost-benefit analysis showed that outpatient management was economically more advantageous than hospitalization and this treatment strategy should be encouraged.[2]

Another decision analysis modeling study conducted by Mission et al.[34] compared treating vs. not treating patients in the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Category 5. Outcomes included preeclampsia, mode of delivery, maternal death, macrosomia, shoulder dystocia, brachial plexus injury (permanent and transient), hypoglycemia, hyperbilirubinemia, and neonatal death. The researchers found that treating GDM patients was cost-effective in terms of improving maternal and neonatal outcomes with an incremental cost of $44203.00/QALY.[34]

Fitria et al.[35] conducted a systematic review of cost-effectiveness studies of GDM treatment published between 2000 and 2017. According to the studies included in the review, GDM treatment could be considered cost-effective but it should be taken into account that all studies were done in high-income countries with obviously different health systems than low-/middle-income countries.[35]

A recent study from China[36] assessed within-trial cost-effectiveness of a shared care program for pregnancy outcomes (individualized dietary advice and physical activity counseling program) compared to usual care, as implemented in a randomized trial of women with GDM. The cost-effectiveness was measured by incremental cost-effectiveness ratio (ICER) in terms of cost per case of macrosomia and large for gestational age (LGA) infant prevented. The economic evaluation included direct (medical and non-medical) costs and indirect costs and was conducted from both a health care system and a societal perspective. The incremental cost of treating a pregnant woman was ¥1877 ($298) from a health care system perspective and ¥2056 ($327) from a societal perspective. The researchers found that lifestyle intervention cost less than ¥33,000 for prevention of a macrosomia/LGA infant. In conclusion, the authors suggest that implementing this lifestyle intervention for women with GDM may be an effective use of health resources.[36]

**Bulgarian experience with pharmacoeconomic studies associated with GDM**

Pharmacoeconomic studies associated with GDM have also been conducted in Bulgaria. They are mainly related to the pharmacoeconomic analysis of the costs and consequences of GDM treatment, as well as to the pharmacoeconomic analysis of the future treatment of T2DM in women with previous GDM.[37,38] All these studies are part of the work.
of Katya Todorova, MD – one of the pioneering endocrinologists in Bulgaria dedicated to the problem of diabetes and pregnancy.

The pharmacoeconomic model for treatment choice in women with GDM considers two therapeutic options – diet treatment alone and a therapy combination of diet and insulin.\[38\] The costs and effectiveness of treatment in terms of metabolic compensation of diabetes and pregnancy outcomes in 50 women with GDM were measured and compared. Patients were divided into 2 groups – 30 women treated with a diet and 20 women treated with insulin. The applied cost-effectiveness analysis showed that despite the higher cost of insulin treatment, it should be preferred as a therapeutic strategy. Based on the obtained results, a decision tree model was built which demonstrated that insulin therapy saves money from the prevention of maternal-neonatal complications that may occur after ineffective diet treatment, amounting to a total of BGN 6954.\[37\]

Pharmacoeconomic analysis for the future treatment of diabetes after GDM is the first prognostic study in Bulgaria that reflects the incidence of diabetes and presents opportunities for future prevention.\[38\] A prophylactic program for diabetes prevention was performed among 50 women with previous GDM. Diabetes has been diagnosed in 13 (26%) out of 50 women with previous GDM in the first year after giving birth. The actual funds spent on the prophylactic program for one woman were BGN 23.50 and BGN 1175.0 for all observed women. Based on the conducted economic analysis, it could be concluded that the preventive strategy for women with previous GDM can reduce the incidence of T2DM for one year by 10% and thus could save real money from prevented morbidity and related treatment unconsumed health expenses.\[38\]

CONCLUSIONS

With its health and economic burden, GDM is a significant challenge for healthcare systems worldwide. The role of pharmacoeconomics is constantly growing due to the limited financial resources in the healthcare system. However, there is a number of difficulties and challenges in conducting pharmacoeconomic studies associated with the financial burden of GDM. Some of these difficulties are related to the presence of pregnancy complications, the unpredictability of pregnancy outcomes, and specific differences in healthcare systems in low- and high-income countries. Efforts should be focused on early diagnosis, prevention of T2DM after birth, as well as prevention of possible complications in children born to mothers with GDM.

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Гестационный сахарный диабет: растущая экономическая проблема

Радиана Стайнова1, Емануела Василева2,4, Веселина Яначкова3

1 Кафедра фармацевтических наук, Факультет фармации, Медицинский университет – Пловдив, Пловдив, Болгария
2 Кафедра пропедевтики внутренних болезней, Факультет медицины, Медицинский университет – Пловдив, Пловдив, Болгария
3 Больница „Д-р Щерев”, София, Болгария
4 Клиника эндокринологии и нарушений обмена веществ, УМБАЛ „Каспела”, Пловдив, Болгария

Адрес для корреспонденции: Радиана Стайнова, Кафедра фармацевтических наук, Факультет фармации, Медицинский университет – Пловдив, бул. „Васил Априлов” № 15А, 4002 Пловдив, Болгария; Email: radiana.staynova@mu-plovdiv.bg; Тел.: +359 32/200 768

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Резюме

Гестационный сахарный диабет (ГСД) является частым осложнением беременности. Последние эпидемиологические данные показали, что распространённость ГСД во всём мире увеличивается. ГСД может привести к неблагоприятным исходам беременности и обычно связан с более высокими затратами на проведение его лечения. В последние годы фармакоэкономика стала важнейшим компонентом систем здравоохранения из-за неуклонно растущих затрат. Несмотря на это, существует несколько фармакоэкономических исследований, оценивающих затраты на беременность, на которую влияет ГСД.

В этой статье представлено краткое введение в фармакоэкономику и рассказывается об экономическом влиянии ГСД. Были проанализированы исследования, связанные с затратами на здравоохранение при ГСД, и была предпринята попытка определить его глобальное экономическое бремя.

Ключевые слова

гестационный диабет, фармакоэкономика, затраты