Commentary

Ethical challenges in gestational diabetes

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Introduction:

Gestational diabetes mellitus (GDM) is a health problem that affects about 7-10% of pregnant women worldwide (1-3). In Iran, the prevalence of GDM is 3.4% on average, and the highest prevalence rates have been reported in Karaj (18.6%) and the lowest in Ardebil (1.3%) (4). The rate is increasing due to the growth in the prevalence of obesity and the age of mothers (5). The growing number of GDM cases is likely to raise ethical and social issues that may have a serious impact on the country's health-care system and impose related burden. Despite the high prevalence of GDM, there are many differences of opinion regarding diagnosis and treatment of this condition, which has caused ethical challenges (6). Through this commentary, we hope to initiate a discussion on some ethical questions that may arise in this field which many clinicians may not be fully aware of them.

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Ethical Framework

Health-care professionals should constantly update their competence in analyzing and resolving ethical problems. In the case of gestational diabetes mellitus (GDM), different ethical frameworks can be used for ethical decision-making. While the ethical issues in this field can be discussed from the perspectives of utilitarian, deontological and virtue ethics, principlism seems to have certain advantages in this regard.

The four principles of "respect for autonomy", "beneficence", "non-maleficence" and "justice" are accepted as the fundamentals of the principlism theory (7). With regard to the principle of "autonomy", Titus states, "*It is therefore imperative that a woman who presents with GDM is counselled extensively during pregnancy in order that she can make an informed choice in the management of her pregnancy*" (8).

While helping people and doing no harm are concepts that trace back to ancient times, they are also emphasized in the utilitarian theory of ethics. Early medical oaths such as those credited to Hippocrates and Maimondies have emphasized these principles as well. However, implications of these two principles in clinical cases such as pregnant mothers with GDM must be thoroughly examined. Beauchamp and Childress propose to acknowledge"non-maleficence" (*not to inflict evil or harm*) and "beneficence" (in three forms: *to prevent evil or harm, to remove evil or harm, and to do or promote good*) (7).

The principle of "justice", which refers to "*fair, equitable, and appropriate distribution in society*" (7), is a complex idea consisting of medical and social paradigms (9). The medical paradigm of justice, which mainly addresses distribution of scarce resources among patients, does not pay enough attention to the social determinants of health. In the case of GDM, although fair access to appropriate services is important, providing the necessary infrastructure for addressing social factors (such as absence of health insurance, poor education, stigmatization, etc.) is crucial. The social paradigm calls attention to social and environmental factors determining the risk for disease, suffering and death in a population. It means that before we ask, "*How should scarce health-care resources be allocated to sick individuals?*" we must ask, for example, "*How does lack of health insurance predict risk of suffering?*" (9).

There may be some conflicts among the ethical principles as well, for instance, none of them

provides a sufficient tool and complete guide to good decision-making in all situations. However, the ethical knowledge of practitioners, their moral sensitivity, and expertise in ethical problem-solving will pave the way for ethical management of the cases.

Social, cultural and religious determinants may also influence decision-making in some cases, but contemporary bioethics tend to emphasize "common morality" in this regard (10-12).

In order to contemplate more on GDM cases, we will discuss specific ethical queries under three subtitles: 1) The benefit/risk ratio and GDM screening, 2) The dilemma of cut-off points, and 3) Limited options for treatment and research during pregnancy

The Benefit/Risk Ratio and GDM Screening

Gestational diabetes exposes mother and fetus to short-term and long-term complications (13). Some potential adverse outcomes in children include: stillbirth, neonatal death, congenital malformations, macrosomia, birth trauma, and shoulder dystocia (14). As for mothers, potential adverse outcomes in the short term include: preeclampsia, gestational hypertension, cesarean delivery, traumatic labor/perineal tears, and postpartum hemorrhage (15), and in the long term, recurrence of GDM, Type 2 diabetes mellitus, hypertension, and ischemic heart disease (16).

According to the above-mentioned evidence, the majority of medical associations recommend universal screening of gestational diabetes during pregnancy (17-19). However, it has been shown that pregnant women who have no risk factor (table 1) do not benefit from screening tests (20).

Table 1. Risk factors of gestational diabetes in pregnant women

- Previous GDM
- An ethnicity with a high prevalence of diabetes
- Maternal age > 35 years
- Family history of diabetes
- First-degree relative with diabetes
- Obesity (BMI > 30 kg/m2)
- Previous macrosomia (birth weight > 4500 g)
- Polycystic ovary syndrome
- Iatrogenic: Glucocorticoids and antipsychotic medication

Taking into account the above-mentioned points, clinicians may face an important moral query about justification of routine screening for all pregnant women. Some believe that increased medicalization of normal pregnancies through universal screening programs may result in more

interventions during labor (inductions and cesarean sections) and even a higher rate of small for gestational age (SGA) babies because of nutritional and treatment approaches (21).

In low-risk cases, the cost of the test and the suffering caused by drinking the glucose solution and the blood-sampling should be discussed with the patient. A very important consideration is that GDM sreening tests may sometimes create psychological stress for pregnant mothers and their families. A competent pregnant woman is capable of making a decision about whether or not to undergo the screening test. On the other hand, a risk-stratified approach may be suggested to improve the overall cost-effectiveness of GDM screening, especially in low-income countries. In the era of precision medicine, it is expected to use more precise measures for analyzing benefits and risks by accounting for individual-level patient characteristics (22). It is noteworthy, however, that balancing the benefits and harms may be a problem for clinicians when the benefit (e.g., mortality reduction) is not commensurate with the risk of harm (e.g., diverting health resources) (23).

There is no doubt that in high-risk cases, the potential complications of undiagnosed gestational diabetes should be clearly discussed with the patient (and her family, if needed). When an informed pregnant woman does not consent to the test, her decision must be respected, but her refusal to consent should be documented in the medical records.

The Dilemma of Cut-Off Points

In addition to diagnostic tests, there is some debate about the cut-off points for these tests, as lower or higher glycemic criteria can be used for diagnosis. The lower glycemic criterion is a fasting plasma glucose level of at least 92 mg per deciliter (≥ 5.1 mmol per liter), a 1-hour level of at least 180 mg per deciliter (≥ 10.0 mmol per liter), or a 2-hour level of at least 153 mg per deciliter (≥ 8.5 mmol per liter). The higher glycemic criterion is a fasting plasma glucose level of at least 99 mg per deciliter (≥ 5.5 mmol per liter) or a 2-hour level of at least 162 mg per deciliter (≥ 9.0 mmol per liter) (24).

Evidence shows that if lower glycemic criteria are used for diagnosis, more pregnant women fall into the category of GDM, while the risk of having a baby with a birth weight above the 90th percentile is the same in both groups (24). Similar to many other diseases, an increase in the number of GDM diagnoses may considerably increase the burden on the national health system. Also, choosing the best treatment should be based on accurate diagnosis. In cases of conflict, a large number of pregnant women will be treated who not only do not benefit

from the treatment, but may even be exposed to side effects, and this clearly contradicts the ethical principle of beneficence and non-maleficence.

It is worth mentioning that in many screening programs, health professionals (and even policy-makers) may overlook the fact that "doing more" does not actually mean "doing better" (23).

Limited Options for Treatment and Research during Pregnancy

The main challenge in gestational diabetes is that there are limited therapeutic options. Despite the existence of a large number of oral agents, treatment is limited to insulin, metformin and glyburide due to the limited clinical research in this area. In fact, insulin is the only medication in the list that has been approved by the FDA. Seeing as pregnant women are a vulnerable group, it seems that such research should be carried out using ethically justifiable criteria and clinical feasibility, and therefore potential fetal-maternal risks limit research in this field. It should be added that a lot of research on GDM cannot be done on animals, which is another reason why research in this area is not adequate.

In order to carry out research on gestational diabetes, as Chervenak and McCullough suggested, there is a need to establish "maternal-fetal intervention clinical centers". These centers would have the mission to conduct both innovation (experiments that are performed for the benefit of an individual patient) and research (experiments that are conducted to create generalized knowledge) within ethical frameworks that ensure the safety of the pregnant mother and the fetus. The goal of these centers would be to develop new treatments for gestational diabetes (25).

Currently, the relative advantages and disadvantages of insulin, metformin and glyburide in the treatment of gestational diabetes are unclear. The long-term consequences of these drugs in children subject to prenatal exposure are unclear, and current guidelines provide contradictory recommendations (26).

The American Diabetes Association (ADA) and the American College of Obstetricians and Gynecologists (ACOG) specify insulin as the first line of treatment (19, 27), while the Society for Maternal Fetal Medicine (SMFM) recommends metformin as a reasonable alternative for women who are unable or unwilling to use insulin (28).

In Iran, insulin is currently the first line of treatment in gestational diabetes because metformin and glyburide pass through the placenta. Pregnant women should be informed about this, even though the short-term consequences of these drugs have not been observed in children subject to

prenatal exposure (29). The ethical principle of respect for autonomy requires the health-care provider to empower the patient to make the right decision about her treatment by giving comprehensive and accurate information.

In the field of treatment, sometimes only one drug can be prescribed, and the health-care provider should explain the clinical benefits and risks of that drug to the patient. However, when there are several medications available for a particular condition, it is the responsibility of the health-care provider to tell the patient about the advantages and risks and recommend the best medication. If none of the medications have a definite advantage over the others, then the choice will be based on the patient's preference.

Sometimes patients are reluctant to accept their health-care provider's recommendations. In such cases, it is important to respect the patient's decision, but to also inform her in more details about the risks of not following the recommendations. The health-care provider should also ask the patient to reconsider her decision for the sake of her own health and that of the fetus. If the patient still refuses the treatment, the health-care provider should document her refusal in the medical records. This will help to protect the health-care provider from any legal liability if adverse outcomes occur (30).

Conclusion

Pregnant women are considered a vulnerable group and therefore specific ethical considerations should be observed in patients with gestational diabetes. The recommendations to these patients should be in accordance with updated scientific evidence and available guidelines for diagnosis and treatment, and their individual autonomy must be respected at all times. To observe the principle of "beneficence", the best interests of the unborn child should also be considered. Other factors that need to be taken into account in health-care system plans include social justice and medical justice.

Considering the differences in the opinions of scientific societies about diagnosis and treatment of gestational diabetes, it seems necessary to establish *mother and fetus research centers* to provide a scientific response to these cases, while considering ethical challenges.

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Conflict of Interests

There are no competing interests to declare.

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