Cuban Contributions to Latin American Clinical Care and Research on Diabetes and Pregnancy

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ABSTRACT
Cuban participation in and contributions to education, medical care and research on diabetes and pregnancy in Latin America dates back to the 1970s when the Latin American Diabetes Association was founded. The Cuban health system and its professionals recognized early the problems presented by diabetes during pregnancy for the health of an expectant mother and her children and assimilated and disseminated important lessons that became influential in the region. These included: importance of adopting a program within primary health care that offers national coverage for diabetic pregnant women, with a special focus on pre-conception monitoring of diabetic women; benefits of defining a specific range for application of a fasting glucose test to identify risk of gestational diabetes through selective screening for the disease; using insulin to treat gestational diabetes; controlling excessive weight at the beginning and during pregnancy; and underscoring the importance of interdisciplinary treatment of diabetes in pregnancy. The goal was to improve care and research in reproductive health for diabetic pregnant women and their children in Cuba.

KEYWORDS: Gestational diabetes, pregnancy, Latin America, Cuba

INTRODUCTION
Systematic activities in specialized medical care and research on diabetes in pregnancy were formalized in Latin America with the creation of the Latin American Diabetes Association (ALAD), founded in 1970 in Buenos Aires, Argentina. ALAD’s mission is to improve the quality of medical care, education and research regarding diabetes mellitus (DM) in the region, including diabetes during pregnancy.[1,2]

When ALAD was founded, morbidity and mortality from diabetes in Latin America was increasing, its steady growth leading to a significant public health problem for the region. Disease prevalence in different countries was reported at 1.2%–7.3%, and PAHO’s Inter-American Investigation of Mortality estimated regional mortality at 2.6% with several countries showing an upward trend.

IMPORTANCE
Cuban professionals have made important theoretical and methodological contributions to the topic of diabetes in pregnancy in Latin America, leading to improved medical care for diabetic pregnant women. This article reviews these contributions and highlights their significance.

Diabetes prevalence in Cuba was 3.8% in 1970 and the mortality rate rose from 2.4 to 10.5 per 100,000 population from 1910 to 1971.[3] While statistics are scarce from those years on diabetes in pregnancy, it was reported that women who were diabetic before becoming pregnant—pregestational diabetes—could present with complications during pregnancy (miscarriages, congenital defects, fetal macrosomia, preeclampsia, fetal death, preterm and dystocic births, etc). It was also reported that such complications were more common in cases when treatment and control of the disease was inadequate.[4–6] In the 1960s, in Cuba and worldwide, diabetes in pregnancy affected approximately 1 in 1000 pregnant women.[7] In 1965, a study conducted in a Cuban maternity hospital corroborated the association between diabetes in pregnancy and fetal mortality.[8]

In the 1990s, gestational diabetes mellitus (GDM) affected a notable proportion of pregnant women in the United States and Latin America, with a prevalence in Latin America ranging from 1% to 14%.[9–11] Cuba’s first study on GDM prevalence, conducted in 1996 in a Havana community polyclinic catchment area, showed that 4.5% of pregnant women there suffered from the disease. While the study’s limited sample could not be used to make inferences regarding national prevalence, it did provide an initial approximation to the problem and suggested that GDM could be a major health challenge for the country.[12] In 2005, WHO reported that GDM was 0.77% in Latin America, while Cuba’s rate was the highest of all countries included in the study (1.75%).[11]

To mitigate this problem, Cuban specialists conducted research and organized specialized health services. They worked to improve the quality of specialized medical care, research and education regarding diabetes in pregnancy through theoretical and methodological contributions.

DEVELOPMENT
When ALAD was founded, specialized medical practice for diabetes in pregnancy had been set up in Cuba; and in the early 1970s the first Diabetes and Pregnancy Service was established at the Ramón González Coro Maternity Hospital.[13] This specialized clinic improved the ability of Cuban specialists to continue making scientific and methodological contributions to the scientific community regarding the care and management of women with pregestational diabetes and GDM.

The founding of a Latin American association where experts from different countries could share information and experiences occurred in a moment when the disease’s prevalence and incidence were rising. This created a favorable context for diabetes in pregnancy to be recognized as a particular problem demanding attention due to its repercussions on the reproductive health of women and the health of their children. Cuban professionals who were diagnosing and treating pregnant women with diabetes and carrying out research on the subject...
appreciated that ALAD offered an opportunity to disseminate the results of their work and extend them to other Latin American countries.

Cuban specialists found that pregnant diabetic women more frequently gave birth to children with congenital malformations (3:1 ratio).[14] Perinatal mortality was also higher among children of women with diabetes in pregnancy.[8,15] Such results confirmed findings by authors in other countries[5,6,16] and enabled researchers to design guidelines for the metabolic and obstetric management of diabetes in pregnant women.[15]

Among these guidelines was insulin as the treatment of choice for diabetes during pregnancy, even if women took oral hypoglycemic drugs before pregnancy. The main argument put forward by the Cuban professionals was evidence of teratogenic effects of some oral hypoglycemic medications such as tolbutamide[17] and occurrence of neonatal hypoglycemia associated with its use, already documented by researchers in other countries.[18] For this therapy, they initially proposed a treatment regimen (pre-hypoglycemic) based on the Roversi gestational diabetes regimen,[19,20] which was later replaced by the intensive or multi-dose insulin treatment plan currently used in Cuba. The regimen consists of administering rapid-action insulin before meals and intermediate-action insulin at night, ensuring optimal glycemic control and best pregnancy outcomes.[21,22] In 2007, ALAD’s Latin American Consensus on Diabetes and Pregnancy (Consenso Latinoamericano de Diabetes y Embarazo de la ALAD) established insulin therapy as the standard for treatment of diabetes during pregnancy.[23]

Cuban specialists participated in preparing ALAD’s clinical care guides for pregnant diabetics, with particular contributions to pre-conception care standards for diabetic women considering pregnancy, as well as control of their diabetes during pregnancy.[24] The theoretical and methodological foundation of Cuban professionals’ contributions arose from their ongoing experience in monitoring and treating diabetic pregnant women in the Diabetes and Pregnancy Service of the Ramón González Coro Maternity Hospital and, from 1992, at the pre-conception care clinic for diabetic women at the Diabetes Care Center of Cuba’s National Endocrinology Institute in Havana.[13]

Among others, their results showed the adverse effects of obesity at the start of pregnancy or excessive weight gain during pregnancy.[25–27] Cuba’s contribution to ALAD’s care recommendations for pregnant diabetics once again consisted of developing guidelines for preconception care for diabetic women.[28] The first reports on the benefits of this care were published in the early 1990s[29–31] and introduced in Cuba in 1992, with the founding of a pre-conception clinic for diabetic women in Havana, the first of this type in the country.[13] Comparing pregnancy outcomes of diabetic women who had received this specialized primary health care and those who had not showed significant differences in prevalence of congenital defects (0.9% vs. 9.6%, respectively) and in perinatal mortality (0.9% vs. 7.0%). Researchers presented new results on the association of initial excess weight (body mass index ≥26.1 kg/m²) and excessive weight gain during pregnancy, with macrosomia and other adverse outcomes for pregnant diabetic women and their newborns. They also suggested preconception care for women with pregestational diabetes, laser therapy to treat diabetic retinopathy during pregnancy, and strict obstetric followup and antepartum fetal surveillance in pregnancies complicated by DM, among other recommendations.[32–34]

The benefits of preconception care, inserted into primary health care, were subsequently extended throughout Cuba, with national coverage of the Cuban Diabetes and Pregnancy Program (PCDE) launched in 2001.[35] Not all Latin American countries were able to establish such services, so Cuba maintained a leading role in management of diabetic pregnancies in the region.

Cuba was also in the leadership of the International Diabetes Federation’s Working Group on Diabetes and Women in the South American/Central American/Caribbean Region when the Latin American and Caribbean Association of Sexual and Reproductive Health in Diabetes was recognized as an International Association of Diabetes and Pregnancy Study Groups (IADPSG)-affiliated scientific organization. Major actions carried out under this leadership include the proposal for Latin American member countries to create national health programs on diabetes and pregnancy, with Cuba’s PCDE as a reference point. This proposal was based on the benefits attained by diabetic Cuban women through attention to the reproductive risk associated with diabetes, including preconception care for diabetic women and transdisciplinary care for pregnant women with diabetes.[13]

In 2007, Cuban specialists proposed ALAD recommend screening for congenital defects in fetuses of diabetic expectant mothers during the first half of pregnancy and for fetal macrosomia from the 28th week, both by ultrasound, as well as periodic obstetric monitoring of fetal health from the 34th week. These recommendations were included in a consensus document. Additional Cuban contributions included emphasis on the benefits of applying WHO’s GDM diagnostic criteria,[23] which were adopted by ALAD with some modifications and are now being implemented.[36] Cuban specialists demonstrated the value of fasting glycemia to screen for GDM and impaired glucose tolerance, in contrast to recommendations from the American Diabetes Association, namely using a glucose tolerance test with a load of 50 g of glucose. The range proposed as a risk marker for the disease was 4.4–5.5mmol/L.[37] This standard was included in the Latin American Consensus on Diabetes and Pregnancy in 2008 and in Cuba’s PCDE disease-screening protocol.[23,35,37]

In 2014, the coverage of the 19 services of the transdisciplinary diabetes care network in pregnancy was 100% of mothers with gestational diabetes; 41% of whom were women undergoing preconception care for pregestational diabetes. Perinatal mortality in children of diabetic mothers was 4.8%, congenital defects appeared in 4.3% of children in the program, and mortality in women with GDM was 24 per 100,000 population. Cuba was recognized by PAHO as one of the few countries in Latin America with a national program that included health promotion activities for diabetic women of reproductive age aimed at preventing GDM and reduce unfavorable pregnancy outcomes, a growing body of research in diabetes.
and pregnancy, and training of some 60 healthcare providers in this field.[38,39]

Cuban specialists showed that GDM also entails high risk of fetal macrosomia (one of the most common complications affecting children of diabetic mothers), and underscored the importance of early GDM diagnosis and intervention during pregnancy to prevent adverse outcomes.[40] They also made the case for diagnostic testing in the 26th week of pregnancy instead of the established practice of testing between the 28th to 32nd week, thus allowing for earlier intervention. This proposal was approved by ALAD[36] and introduced in Cuba in 2017.[41]

In 2015, newborns of Cuban diabetic mothers had a low percentage of congenital defects (2.5%). Perinatal mortality was also low (2.9%) for newborns of women with pregestational diabetes (2008–2015). Other events with low relative frequencies in women with GDM in 2015 were: fetal macrosomia (6.0%), premature births (3.1%), low birth weight (4.0%), perinatal mortality (0.6%), and maternal mortality (0.0%). Today, Cuba remains one of the few countries in Latin America with consistent and systematic preconception care, since the PCDE provides preconception care for women with pregestational diabetes, and prenatal care for diabetic women, diagnosis of GDM, and long-term monitoring of these women and their children.[42]

CONCLUSIONS

Cuban specialists have played an important role in early detection and prevention of congenital defects in children of diabetic mothers and on strict obstetric monitoring, prenatal fetal surveillance and identification of risk factors for fetal macrosomia, the most common complication in diabetic pregnancies. They recommended use of insulin for diabetic pregnancy management with specific treatment plans and promoted preventive use of insulin therapy in GDM. This contributed to significant improvements in health indicators of diabetic pregnant women in Cuba. Cuban proposals also led to new regional consensus recommendations in areas such as weight control according to initial weight and weight gain, as well as new guidelines for applying fasting blood glucose tests to screen for GDM.

The organization of health services under a specific national diabetes and pregnancy program inserted into primary health care proved to be an effective strategy in monitoring and controlling diabetes before conception, during pregnancy, and up to the time of delivery, an experience shared regionally.

Through dissemination of their research results and knowledge gained from their experience in management of women of childbearing age and diabetic women during pregnancy, Cuban specialists have made important contributions to defining standards and procedures to ALAD's, in treatment of diabetic pregnant women.

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