

Changes in medication initiation and selection patterns for gestational diabetes management

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Abstract

Recent trends regarding GDM medication use have not been well described in prior literature. We identified pregnant patients enrolled in Tennessee Medicaid with a GDM diagnosis who delivered in 2007 to 2019. We studied initial GDM medication use by delivery year (overall and by medication type). Over twenty percent of patients filled at least one prescription for GDM medication in the study period, with a significantly increasing prescribing trend over time. Starting in 2016, metformin replaced glyburide as the most common medication prescribed, which corresponds temporally with the emergence of evidence on the safety and effectiveness of different oral hypoglycemic medications and related changes in ACOG practice recommendations. These findings highlight how practice patterns have potential to shift quickly in response to evolving data.

TITLE PAGE

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ABSTRACT: Recent trends regarding GDM medication use have not been well described in prior literature. We identified pregnant patients enrolled in Tennessee Medicaid with a GDM diagnosis who delivered in 2007 to 2019. We studied initial GDM medication use by delivery year (overall and by medication type). Over twenty percent of patients filled at least one prescription for GDM medication in the study period, with a significantly increasing prescribing trend over time. Starting in 2016, metformin replaced glyburide as the most common medication prescribed, which corresponds temporally with the emergence of evidence on the safety and effectiveness of different oral hypoglycemic medications and related changes in ACOG practice recommendations. These findings highlight how practice patterns have potential to shift quickly in response to evolving data.

INTRODUCTION: The reported frequency of medication management for gestational diabetes mellitus (GDM) varies widely in prior studies (8-56%) depending on study population and research approach. {Camelo Castillo, 2014 #205} Yet, few studies have examined recent trends in medication preference for GDM management. {Camelo Castillo, 2014 #205} We examined changes in GDM medication use over time among Tennessee Medicaid (TennCare) recipients.

METHODS: We identified pregnant patients with a diagnosis of GDM, aged 15-44 years, and enrolled in TennCare who delivered a live infant between 2007-2019. Patients with type 1 and 2 diabetes, hypoglycemic medication prescriptions filled prior to GDM diagnosis, and GDM prescriptions filled for medications other than metformin, insulin, or glyburide were excluded. Data were derived from TennCare files linked to birth certificates and a statewide hospitalization registry. Filled prescriptions for GDM medications were used as a proxy for medication use. We identified the initial GDM medication filled after GDM diagnosis and used logistic regression to assess the association between delivery year and any GDM medication use accounting for maternal age, body mass index (BMI), race and ethnicity, residential distance from delivery facility, and facility. We also examined changes in use of specific GDM medications over time. The study was approved by our institution's and the Tennessee Department of Health's Institutional Review Boards, with exemption for informed consent given the large number of cohort patients and the retrospective nature of our study.

RESULTS: Among 32,793 pregnant patients with GDM included in the study, mean maternal age was 26.8 (± 5.8) years and BMI was 30.3 (± 8.4) kg/m² at delivery. Overall, 6,617 (20.2%) initiated pharmacotherapy for GDM with either metformin (34.9%), insulin (21.5%), or glyburide (43.6%). During the study period, GDM medication use increased over time from 17% in 2007 to 28% in 2019, with later years associated with higher odds of medication use while adjusting for well-known predictors of medication use including maternal age (adjusted odds ratio [aOR]: 1.06, CI 1.05-1.06) and BMI (aOR 1.06, CI 1.06-1.06). Substantial changes in selection of initial GDM medication were also observed over time. In 2007, most patients used glyburide (45.8%) or insulin (40.0%) and fewer used metformin (14.2%). Metformin use surpassed glyburide after 2016, with most patients receiving metformin in 2019 (63.2%) followed by insulin (27.5%) and glyburide (9.3%) (Figure). No relevant changes in TennCare medication formulary occurred during the study period.

CONCLUSION: The prevalence of medication use among GDM patients in Tennessee Medicaid has increased over time, with metformin now the most commonly initiated GDM medication.

In a recent study of commercially insured beneficiaries, Venkatasht et al. also observed substantial changes in GDM pharmacotherapies from 2015 to 2018, noting a shift from glyburide to insulin as the most common initial treatment for GDM.¹ In contrast, our study in a Medicaid population determined that metformin has replaced glyburide as the most used initial medication. These discrepant findings suggest possible differential prescribing based on socioeconomic status or regional differences in prescribing preferences. Nevertheless, the changes observed in our Medicaid study align temporally with emerging evidence on the safety and effectiveness of oral hypoglycemic medications²⁻⁴ and corresponding changes in the American College of Obstetricians and Gynecologists (ACOG) practice recommendations,⁵ highlighting how practice patterns can shift quickly. Taken together, these studies underscore the need for additional assessments of factors that influence pharmacotherapy selection for GDM management, as well as the clinical impact of prescribing pattern changes on perinatal outcomes and healthcare costs.

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CONTRIBUTION OF AUTHORSHIP: AP, ADW, AJS, CGG, and SSO were all instrumental in the conception, planning, and carrying out this study. AP, ADW, AJS, SEP, and SSO were responsible for the data analysis. AP and RS were responsible for writing up this research letter and all other co-authors, specifically MAA, CGG, and SSO were part of the editing process prior to submission.

ETHICS APPROVAL: The study was approved by the Vanderbilt University Medical Center (IRB # 190068, approval date 1/18/2019) and the Tennessee Department of Health (IRB # TDH IRB 2019-0099, approval date 5/10/2021) Institutional Review Boards.

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REFERENCES:

1. Venkatesh KK, Chiang CW, Castillo WC, et al. Changing patterns in medication prescription for gestational diabetes during a time of guideline change in the USA: a cross-sectional study. *BJOG*.2022;129(3):473-483.
2. Balsells M, Garcia-Patterson A, Sola I, Roque M, Gich I, Corcoy R. Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis. *BMJ*.2015;350:h102.
3. George A, Mathews JE, Sam D, et al. Comparison of neonatal outcomes in women with gestational diabetes with moderate hyperglycaemia on metformin or glibenclamide—a randomised controlled trial. *Aust N Z J Obstet Gynaecol*. 2015;55(1):47-52.
4. Camelo Castillo W, Boggess K, Sturmer T, Brookhart MA, Benjamin DK, Jr., Jonsson Funk M. Trends in glyburide compared with insulin use for gestational diabetes treatment in the United States, 2000-2011. *Obstet Gynecol*. 2014;123(6):1177-1184.
5. ACOG. ACOG Practice Bulletin No. 190: Gestational Diabetes Mellitus. *Obstet Gynecol*. 2018;131(2):e49-e64.

FIGURE LEGEND

Figure: Trends in initial GDM medication prescription (Glyburide, Metformin, or Insulin) by delivery year among pregnant Tennessee Medicaid patients with GDM, 2007 - 2019 (N=6,617)

*Delivery year significantly associated with increase in odds for medication initiation when adjusting for *a priori* selected variables including, maternal age (years), body mass index at delivery (BMI, kg/m²), race and ethnicity (White, Black, Hispanic, Asian, and other), distance from delivering facility (miles), and facility (*p* -value considered significant when *p* <0.05).

Figure. Trends in initial GDM medication prescription (Glyburide, Metformin, or Insulin) by delivery year among pregnant Tennessee Medicaid patients with GDM, 2007 - 2019 (N=6,617)

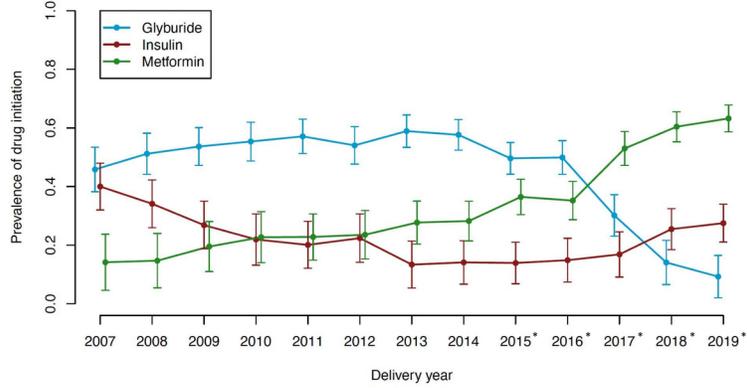


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