

Adherence to Clinical Practice Guidelines during Antenatal Management of Gestational Diabetes Mellitus: An Integrative Review

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Abstract

The number of pregnant women affected by gestational Diabetes (GDM) is increasing globally with an estimated prevalence as high as 15%. Gestational Diabetes Mellitus is associated with birth complications for women and newborn, includes development of type II diabetes, preeclampsia during pregnancy, increasing the risk of fetal loss, stillbirth and perinatal death. An integrative literature review applied, systematic search from different data base obtained from international and middle east countries to assess adherence level of guidelines. Clinical guidelines are set to ensure and assure homogeneity as well as the quality of provision of care. National and international consensus has yet to be achieved in the management of diabetes in pregnancy, adherence of recommended antenatal care content to a minimum level appears to be unmet. Complete provider adherence to first antenatal guidelines was 48.1%, Guideline dissemination alone does not change practice; assessment of barriers/enablers and implementation is important. Guidelines are useless when they are not used or adhered to. Each guideline needs an **Appendix** on how adherence has to be measured, there is a need for some uniformity across guidelines to measure adherence. Diabetes management is an essential constituent to prevent prognosis of diabetes complications.

Keywords

Adherence, Antenatalcare, Clinical Practice Guidelines, Gestational Diabetes Mellitus

1. Introduction

Quality of care can be improved by decreasing unnecessary practice variation

between professionals. One way to reduce practice variation is by moving evidence-based knowledge into daily practice. To facilitate the translation of the most recent evidence into practice, guidelines are developed and implemented [1].

Clinical guidelines are set to ensure and assure homogeneity as well as the quality of provision of care. Utilization of guidelines is influenced by many factors. Clinical practice guidelines are “statements that include recommendations intended to optimize patient care that is informed by a systematic review of evidence and an assessment of the benefit and harms of alternative care options”. Guidelines contain practical evidence-based advice for professionals and patients and aim to improve the quality of care, guidelines are useless when they are not used or adhered to [1].

Adherence has been defined as “conformity to, accomplishing or following official or institutional requirements, guidelines, protocols, recommendations or standards” [2].

Antenatal care (ANC) is an effective measure that provides care to the pregnant women, quality is still a problem. Quality in maternal services involves providing a minimum level of care to all pregnant women, yet adherence of recommended ANC content to a minimum level appears to be unmet, adherence to clinical guideline is important especially in pre gestational complication like gestational diabetes mellitus [3].

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy, and it is associated with several maternal and fetal effects includes development of type II diabetes, preeclampsia during pregnancy, increasing the risk of fetal loss, stillbirth and perinatal death [4] [5].

Globally GDM complicate about 1% - 14% of all pregnancies, the prevalence rate in most European countries including United Kingdom is about 1% - 2% while among Asian women prevalence rate was higher nearly 11.9% especially Chinese and Indian women [6]. The prevalence of Diabetes in the Palestinian population in the West Bank, Gaza and E. Jerusalem is high around 15.3%, average prevalence of GDM in Gaza was 1.8% and is increasing [6] [7].

The aim of this literature review was to critically analyze data from existing studies and explore the themes identified in relation to the adherence to clinical guideline during antenatal management of GDM, focus on assessment to adherence international and national level, the problem her according to literature non-adherence to clinical guidelines. Adherence has critical role in the determination of therapeutic outcomes and is considered a key factor in achieving therapeutic success. Therefore, a need to investigate this problem in our country exists. Guideline dissemination alone does not change practice; assessment of barriers/enablers an implementation design must be theory-driven [8].

2. Materials and Methods

In this review, the search was performed by different international databases in-

cluding: Google Scholar, PubMed, Medline, CINAHL, EBSCO and the Jordanian Database for Nursing Research using the keywords of “adherence”, “clinical practice guidelines”, “antenatal care”, “gestational diabetes mellitus”, “prenatal care”. These words were searched in combination with each other and in separated form. For example, during the initial search, the keyword “adherence” was combined with “clinical practice guideline”. Later, during each new search a new keyword added until including all keywords in the last search. However, the searching process was limited to following inclusion criteria: full text, written in English, published between 2008 and 2018, and specifically related to adherence to clinical guidelines during GDM treatment in antenatal care.

However, review papers and incomplete reports in the form of editorials, opinion pieces, and conference abstracts have been excluded. Furthermore, a total of 1260 articles were retrieved and after removing the duplicated articles 900 articles remain, the initial evaluation for their titles abstracts took place, 579 excluded by title, 276 excluded by abstract, only 45 were found to be related to the topic of interest. Then, related articles were printed and read in full, following a secondary evaluation, 15 articles were exactly identified to cover the inclusion criteria. As a result, those fifteen articles were included in this review (**Figure 1**).

3. Results

Fifteen relevant articles have been reviewed. From each article the following data have been extracted: Title, author, study purpose, design, sitting and findings.

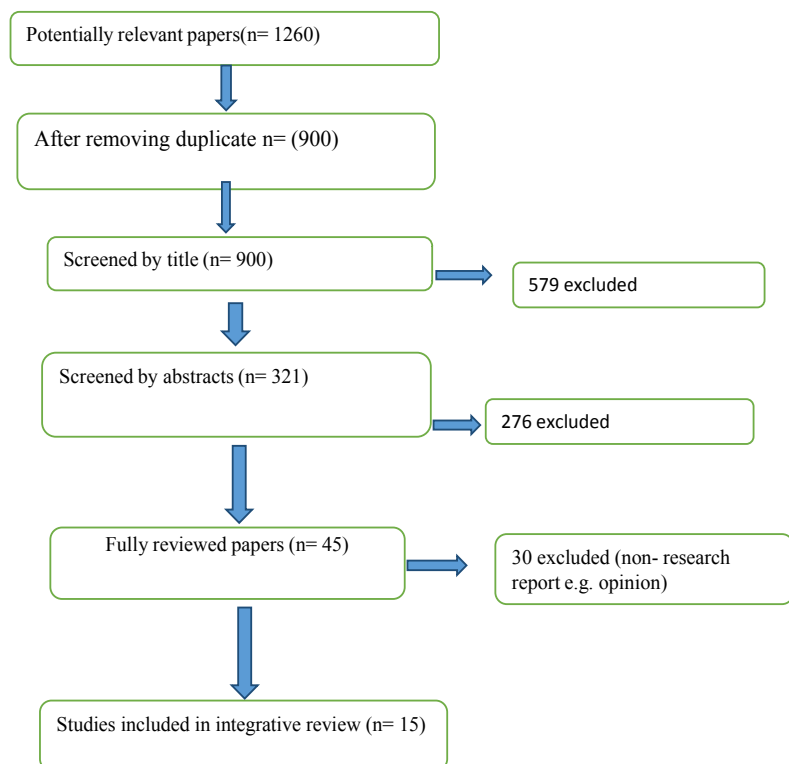


Figure 1. Search strategy and outcomes. PRISMA guideline.

Then, the authors compared articles, interpreted findings to identify themes, and grouped them based on their similarities. Overall, the fifteen reviewed research articles published between 2008 and 2018 (three systematic review, eight cross sectionals quantitative study, one survey study and three descriptive). All articles presented in **Appendix**.

On the international level two study was conducted in Ghana, two study was conducted in Australia, one study was conducted in Malaysia, one study was conducted in each of Sweden, Netherlands, Korea. In the Middle East country one study was conducted in Riyadh, Saudi Arabia the other in Morocco, the third one in Palestine, the reaming studies was systematic review done in different countries. However, to address the purpose of this review, the findings (highlight adherence to clinical practice guidelines) were categorized into common themes, using a color-coding method to highlight similarities across the literature. After sorting and grouping the data, three thematic areas were identified these includes the following: adherence to clinical practice guidelines in GDM patient's; barriers and enablers, adherence to clinical GDM guidelines in studies from international countries, adherence to clinical GDM guidelines in studies from middle east countries.

3.1. Theme One: Adherence to Clinical Practice Guidelines in GDM Patient's Barriers and Enablers

Diabetes is a global health problem, in both developed and developing countries, the prevalence of gestational diabetes (GDM) in low and lower middle income countries (LLMIC) is increasing. Although its associated with short and long term complications for mothers and their newborns, there is a lack of knowledge about how to detect and manage GDM. Although, guidelines for GDM screening and management are available and freely downloadable from the internet from high income setting, there is a lack of knowledge about the degree to which guidelines developed in high income settings are appropriate for use in low income settings or less developed countries, where resources are scarce and access to care is limited [9] [10].

Four studies about management of GDM in low and lower middle income country in Africa, South Asia, and Latin America. The results demonstrated high diversity in screening and management practices.

According to Utz, Kolsteren [11] they stated that management of GDM was found to take place mainly at the tertiary level, A cross-sectional survey was conducted between November 12, 2014 and May 11, 2015. Questionnaires were distributed to gynecologists, medical doctors and endocrinologists who were involved in providing care to patients with GDM. Questionnaires were sent to 182 individuals and 77 healthcare providers from 26 countries completed the survey. The results demonstrated high diversity in screening and management practices. Only 52 (68%) participants reported that any guidelines were available in their setting.

According to Utz, Delamou [12], there is a lack of knowledge on how the women with GDM are managed in low resource settings. A scoping review conducted of published literature, all articles containing information on clinical practices of detection and management of gestational diabetes published until April 24, 2016 included. Results: 23 articles identified mainly from Asia and sub-Saharan Africa. All studies show that lack of uniformity in the management of gestational diabetes requires a focus on the promotion of universal guidelines on GDM screening and management that are applicable to low resource settings.

3.1.1. Barriers to Adherence

According to Utz and De Brouwere [10], both providers and patients poses a substantial barrier to detection and management of GDM due to unavailability of guidelines combined with lack of knowledge about GDM, leading to deficiencies in screening and counseling. Additional expenses related to specific tests and changes in diet were identified as important challenges, limited access to regular monitoring and follow-up care as a result of distance and costs are also considered. Services were not available at all levels nor was adequate testing equipment. Lack of communication and collaboration between different specialists and treatment delays as a result of patients being seen by multiple providers.

According to [8], reasons for failure to adhere to best practice are multifactorial and include: unfamiliarity with Nutrition Practice Guidelines Among relevant staff; insufficient dietetic resources; and women's lack of awareness of the benefits of regular dietetic counselling. Barriers have been grouped into the theoretical domains of: Knowledge; Beliefs about consequences; Intentions; Social influences; Social/professional role and identity; Environmental context and resources; and Memory, attention and decision processes.

Four main categories of barriers to physician guideline adherence:

- 1) The payment system; Lack of uniformity leads to diffusion of the effects of Pay for Performance programs.
- 2) Lack of information technology systems; Insufficient access to guidelines at the point of care
- 3) Physician culture, beliefs and habits; physicians base clinical decisions on their personal experience, physicians generally believe that their own clinical practice is good
- 4) The guideline development process and utility and function, development process of guidelines presents their own obstacles to adherence, mainly:
 - a) The lack of sufficient flexibility and relevance to physician practice; and
 - b) The lack of transparency in guideline development [13].

3.1.2. Enablers and Strategies to Adherence

Adherence to guidelines is associated with better outcomes among patients with gestational diabetes. Enablers, identified through clinic observation and team discussion, project funding for dietetic clinic time, a positive research and audit culture of the organization. To improve adherence many strategies includes Engage physicians in guideline development and review process; Expedite new re-

search to support guideline development; and Make guidelines actionable [8] [13].

According to previous studies guidelines dissemination alone does not change practice; assessment of barriers/enablers and implementation design must be theory-driven. Policy makers need to address these challenges by strengthening their health care system as a whole, relevant and effective strategies to apply guidelines in clinical practice are needed to improve patient outcomes.

3.2. Theme Two: Adherence to Clinical GDM Guidelines in Studies from International Countries

According [2] [14] guidelines are developed to ensure quality, uniformity and consistency of care for clients. Engagement of providers during the process of developing guidelines is important in ensuring that they adhere to the guidelines. There is discrepancy between provider knowledge and practice, especially in low and middle income settings, and reasons for this need to be explored. In a two study in Ghana, a cross-sectional analysis of a prospective cohort study on adherence to guidelines was carried out. Complete provider adherence to first antenatal guidelines was 48.1%. Complete provider adherence to first antenatal visit guidelines is low across different facilitytypes in the Greater Accra region of Ghana, providers should be trained to adhere to the guidelines during provision of care to all pregnant women since adherence to the guidelines at first visit play a major role for the quality of care of the pregnant woman.

In Australia according to [8] [15] one study was conducted in two developed high-income countries to compare Austrian and Australian national guidelines for gestational and pre-gestational diabetes and evaluate the level to which physicians comply with their country's guideline. The other one to identify barriers and enablers that confront GDM management and treatment. When guidelines compared between Austrian (ÖDG, Austrian Diabetes Society) and Australian guidelines (ADIPS, Australasian Diabetes in Pregnancy Society), they show that National and international consensus has yet to be achieved in the management of diabetes in pregnancy.

Several studies was done by [3] [9] [16] [17] In Malaysia , Korea, Netherlands, Sweden ,all studies focus on adherence to clinical practice guidelines ,focus on adherence to antenatal guidelines during GDM care and outcomes in patients. Result show many different ways to measure adherence, adherence to guidelines varies widely. Adherence is positively related to: evidence base of guideline, practicality of guideline, automated support system, a positive attitude of professionals.

3.3. Theme Three: Adherence to Clinical GDM Guidelines in Studies from Middle East Countries

There is a lack of study about adherence to clinical practice guideline for treatment of GDM in middle east countries. Diabetes in the Middle East: over the past two decades, there had been changes in the lifestyle of eastern Mediterra-

nean countries, this led to an increase in non-communicable diseases, such as hypertension, cardiovascular diseases and diabetes mellitus.

In a study done in Egypt, using cross-sectional design, the glycemic control and prevalence of microvascular and neuropathic complications were described among Egyptians with diagnosed diabetes. The results were; blindness 5%, 21% albuminuria, 42% had retinopathy, 22% neuropathy, clinical nephropathy prevalence was 7%, foot ulcers were only 1%. Other studies were made in Egypt and Jordan to measure the prevalence of obesity and related diabetes. The results from Egypt were; 16% were obese and 4.9% had diabetes [18].

Albarrak, Mohammed [19] conducted a study to assess diabetes care in primary clinics based on the guidelines of American Diabetes Association (ADA). A retrospective study of medical records and laboratory system was conducted between November 2011 and May 2012. In total, 200 diabetic patients from the database of Primary Care Clinics (PCCs) in King Khaled University Hospitals (KKUH) were randomly selected. Study revealed insufficiency of diabetes care, and proper guidelines are not followed in the care for diabetic patients in the PCCs in comparison to the ADA standards of care.

Utz, Assarag [20] conducted a study in Morocco to assess knowledge and practices of general practitioners, midwives and nurses working at primary health care facilities regarding screening and management of gestational diabetes (GDM). Antenatal care (ANC) attendance is high, first level health care providers, mainly nurses and midwives, are usually the first point of contact for pregnant women. Result show that public primary health care providers have a basic understanding of GDM but screening and management practices are not uniform. Most nurses and midwives lack pre-service training on gestational diabetes while 56.8% of the doctors had some pre-service training. After diagnosing GDM, 88.5% of providers refer patients to specialists, only 11.5% treat them as outpatients.

In Gaza strip in Palestine a study was conducted by Radwan, Elsous [21] to assess the level of good glycemic control, to examine factors influencing good glycemic control and to determine association between adherence to antidiabetic medications and glycosylated hemoglobin (HbA1c). A cross-sectional design was employed among 369 patients with type 2 diabetes mellitus (T2DM). study showed that glycemic control was suboptimal. To improve glycemic control and prevent diabetes-related complications it's important to get Knowledge of factors associated with that were: older age, high medication adherence, and better health literacy.

4. Discussion

The current review showed that Gestational Diabetes Mellitus management is an essential constituent to prevent prognosis of GDM complications. The prevalence of gestational diabetes (GDM) in low and lower middle income countries (LLMIC) is increasing. These findings could provide valuable evidences to enhance concept of adherence to guidelines in international and middle east coun-

tries for GDM women. The findings were clustered in three themes as following adherence to clinical practice guidelines in GDM patient's; barriers and enablers, adherence to clinical GDM guidelines in studies from international countries, adherence to clinical GDM guidelines in studies from middle east countries.

Fifteen studies conducted in the international level and middle east countries level to assess level of adherence to clinical practice guidelines in management and treatment of GDM, most of studies are cross sectional studies show no uniformity across guidelines so adherence more difficult to measure. Guidelines dissemination alone does not change practice, it's important to develop a monitoring system and specific method to measure adherence. Many barriers and challenges that face health care providers to adhere to clinical guidelines one of them Lack of resources, insufficient dietetic resources; and women's lack of awareness of the benefits of regular dietetic counselling, Physician culture, beliefs and habits.

Providers should be trained and supported to adhere to the guidelines during provision of care to all pregnant women.

No studies about adherence to clinical guidelines in Jordan or Palestine. In middle east countries in Morocco, Saudi Arabia two studies was conducted about Knowledge and practice related to gestational diabetes among primary health care providers, Evaluation of diabetes care management in primary clinics based on the guidelines of American Diabetes Association respectively. Further studies needed to assess adherence level of guidelines during antenatal care for GDM patients especially in developing countries.

5. Conclusions

To achieve a high quality of GDM management, national guidelines must be consistent and uniform; it must be integrated into local care processes. Adherence to clinical guidelines decrease prognosis of GDM complications. Complete provider adherence to first antenatal visit guidelines is low across different facility. Providers should be trained and supported to adhere to the guidelines during provision of care to all pregnant women.

An essential element in the success of the management plan is diabetes management standards. Most of the elements examined are not in full compliance with the ADA standard. Continues monitoring and self-review are recommended. There is a need of actions improving compliance to the local guidelines. Many barriers and enablers or facilitators to adherence present, we should consider it and try to overcome barriers in order to improve adherence to clinical guidelines and then improve quality of care and patient health.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

Title	Author(s)	Purpose	A design	Sitting	Result
Evaluation of diabetes care management in primary clinics based on the guidelines of American Diabetes Association	Albarrak, Mohammed [19]	The main objective of this study was to assess diabetes care in primary clinics based on the guidelines of American Diabetes Association (ADA).	A retrospective study at King Khaled University Hospitals	Riyadh, Saudi Arabia.	The result showed that elements achieving the ADA targets for overall care were medical history (44.9%), physical examination (59.6%), laboratory valuation (36.3%), and referrals (19.3%). The other subelement indicators such as referral to diabetes self-management education clinics (10%), dental examination (2%), HbA1c regular monitoring (33.5%), and blood pressure determination (100%) were documented with adherence to ADA standards.
Public health facility resource availability and provider adherence to first antenatal guidelines in a low resource setting in Accra, Ghana	Amoakoh-Coleman, Agyepong [14]	aim was to describe public health facility resource availability in relation to provider adherence to first antenatal visit guidelines.	A cross-sectional analysis of the baseline data of a prospective cohort study was carried out in 11 facilities in the Greater Accra Region of Ghana.	Ghana.	Eleven facilities comprising 6 hospitals (54.5%), 4 polyclinics (36.4%) and 1 health center were randomly sampled. Complete provider adherence to first antenatal guidelines for all the 946 participants was 48.1% varying significantly amongst the types of facilities, with highest rate in the polyclinics.
Client Factors Affect Provider Adherence to Clinical Guidelines during First Antenatal Care	Amoakoh-Coleman, Agyepong [2]	Our objectives were to determine the level of provider adherence to first antenatal visit guidelines in the Safe Motherhood Protocol (SMP), and assess patient factors that determine complete provider adherence.	Cross-sectional study is part of a cohort study that recruited women who delivered in eleven health facilities and who had utilized antenatal care services during their pregnancy in the Greater Accra region of Ghana	Ghana.	Complete adherence to guidelines pertained to only 48.1% of pregnant women. Providers were significantly more likely to completely adhere to guidelines when caring for multiparous women but less likely to do so when attending to women with history of previous pregnancy complications
Knowledge and practice related to gestational diabetes among primary health care providers in Morocco: Potential for a defragmentation of care?	Utz, Assarag [20]	The objective of this study was to assess knowledge and practices of general practitioners, nurses and midwives working at primary health care facilities in Morocco regarding screening and management of gestational diabetes (GDM).	Structured interviews with 100 doctors, midwives and nurses at 44 randomly Selected public health Care centers were conducted in Marrakech and Al Haouz. All data Were descriptively analyzed.	Morocco:	Public primary health care providers have a basic understanding of gestational diabetes but screening and management practices are not uniform. Although 56.8% of the Doctors had some pre-service training on gestational diabetes, most nurses and midwives lack such training
“Why screen if we cannot follow-up and manage?” Challenges for gestational diabetes screening and management in low and lower-middle income countries: results of a cross-sectional survey	Utz and De Brouwere [10]	The objective of our study was to identify the challenges that first line healthcare providers in LLMIC face in screening and management of GDM.	We conducted a cross-sectional survey of key informants from 40 low and lower-middle income by sending out questionnaires to 182 gynecologists, endocrinologists and medical doctors	Africa, South-Asia and Latin-America	Unavailability of guidelines combined with lack of knowledge about GDM on the part of both providers and patients poses a substantial barrier to detection and management of GDM, leading to deficiencies in screening and counseling.
Detection and Management of Diabetes during Pregnancy in Low Resource Settings: Insights into Past and Present Clinical Practices	Utz, Delamou [12]	To identify modalities of gestational diabetes detection and management in low and lower middle income countries.	a scoping review was conducted of published literature and searched the databases all articles published until April 24, 2016 included.	Asia and sub-Saharan Africa.	23 articles were identified mainly from Asia and sub-Saharan Africa. The majority of studies were conducted in large tertiary care centers and hospital admission was reported in a third of publications.

Continued

Clinical article: A snapshot of current gestational diabetes management practices from 26 low-income and lower-middle-income countries	Utz, Kolsteren [11]	To identify screening and management practices for gestational diabetes mellitus (GDM) in low-income and lower-middle-income countries.	A cross-sectional survey was conducted between November 12, 2014 and May 11, 2015. Questionnaires were distributed to who were involved in providing care to patients with GDM in low-income or lower-middle-income countries in Africa, South Asia, and Latin America.	Africa, South Asia, and Latin America.	Questionnaires were sent to 182 individuals and 77 healthcare providers from 26 countries completed the survey. The results demonstrated high diversity in screening and management practices. Only 52 (68%) participants reported that any guidelines were available in their setting.
Barriers and enablers to translating gestational diabetes guidelines into practice	Wilkinson, McCray [8]	Analyze Barriers and enablers to translating gestational diabetes guidelines into practice	the outline recommended by French <i>et al.</i> that involved four steps to assess influencing factors and design of implementation strategies in a translational research project was followed	Australia	Of 44 clinic staff surveyed, most believed regular dietetic contact could influence diet, but fewer believed contact could influence blood glucose level (BGLs), pharmacotherapy, and care costs, and only half felt contact could influence weight gain or macrosomia
Surprisingly low compliance to local guidelines for risk factor based screening for gestational diabetes mellitus—A population-based study	Persson, Winkvist [17]	To investigate: 1) the compliance with local guidelines of screening for GDM and 2) the outcomes of pregnancy and birth in relation to risk factors of GDM and whether or not exposed to oral glucose tolerance test (OGTT).	population-based retrospective cross-sectional study of 822 women. A combination of questionnaire data and data collected from medical records was applied.	Sweden	31.3% women fulfilled at least one criterion for being exposed to screening for GDM according to the local clinical guidelines. However, only 30.7% of these women were actually exposed to OGTT and of those correctly exposed for screening, seven women were diagnosed with GDM.
Assessing the Extent of Adherence to the Recommended Antenatal Care Content in Malaysia: Room for Improvement	Yeoh, Hornetz [3]	Analyze adherence to recommended antenatal care (ANC); specifically, to examine the extent of adherence to recommended ANC content and to determine the factors influencing ANC content score.	A retrospective cohort study of 522 randomly selected women who used ANC was conducted.	Malaysia	Around half of the women had <80% of recommended ANC content documented. Health education had the lowest mean score, at around 35%. The low-risk pregnancies had a higher ANC content score than the high-risk pregnancies (78% vs. 75%; P = 0.002).
Management of diabetes in pregnancy: comparison of guidelines with current practice at Austrian and Australian obstetric center	Zeck, Panzitt [15]	To compare Austrian and Australian national guidelines for gestational and pre-gestational diabetes and estimate the level to which physicians comply with their country's guidelines.	Austrian (ODG, Austrian Diabetes Society) and Australian guidelines (ADIPS, Australasian Diabetes in Pregnancy Society) for the treatment of gestational diabetes and pre-gestational diabetes were systematically reviewed.	Australia Austrian	More variation was found in the management of gestational than pre-gestational diabetes. There were differences in oral glucose tolerance test and cut-off levels for diagnosing gestational diabetes in both centers and guidelines.
Guideline adherence in the Netherlands: a systematic review	[16]	To investigate the adherence rate to Dutch guidelines, the influential factors to it and the effects of it	Systematic Review	Netherlands	5 categories of influential factors for adherence: 1) Health care professional 2) Guideline 3) Organization/system 4) Implementation 5) Patient
Sustainability of professionals' adherence to clinical practice guidelines in medical care: a systematic review	[1]	To evaluate 1) the state of the art in sustainability research and 2) the outcomes of professionals recommendations in medical practice	Systematic Review		The search retrieved 4219 items, of which 14 studies met the inclusion criteria, involving 18 sustainability evaluations.

Continued

<p>Adherence to clinical practice guidelines and outcomes in diabetic patients</p>	<p>[9]</p>	<p>To examine the level of adherence to clinical practice guidelines and its relationship to outcomes in patients with diabetes. a</p>	<p>Retrospective cohort study</p>	<p>Korea</p>	<p>Testing rates for blood pressure, eye examination, HbA1c, renal function and lipid profiles were 93.9%, 32.8%, 84.9%, 33.5% and 45.9%, respectively. The adherence to recommendations was unsatisfactory.</p>
<p>Glycemic control among primary care patients with type 2 diabetes mellitus in the Gaza Strip, Palestine</p>	<p>[21]</p>	<p>to assess the level of good glycemic control, to determine association between adherence to antidiabetic medications and glycosylated hemoglobin (HbA1c) and to examine factors influencing good glycemic control.</p>	<p>A cross-sectional design was employed among 369 patients with type 2 diabetes mellitus (T2DM)</p>	<p>Gaza Strip, Palestine</p>	<p>Mean of HbA1c was 8.97 (2.02) and one fifth of patients had good glycemic control (HbA1c ≤ 7%). Factors associated with good glycemic control were: older age, high medication adherence and better health literacy</p>