A comparative review of the current management guidelines in type 2 diabetes mellitus

Subham Das, Abheek Das

ABSTRACT

Background: Diabetes mellitus is a modern day epidemic, majority of the cases belonging to type 2. In spite of having many different guidelines given by many professional bodies as to the screening, diagnosis, and management of diabetes and related complications, physicians all over the globe are yet to reach a clear consensus regarding the same. **Objective:** With this background knowledge, the objective of the present review is to find out the areas of common consensus among various popular guidelines regarding type 2 diabetes mellitus, and more importantly, the aspects of various guidelines where there is significant disagreement among the guidelines. **Method:** Various popular diabetes-related guidelines given by WHO, ADA-EASD position statement, AACE, etc. were reviewed and the various aspects of their guidelines, especially the area where the guidelines are in disagreement among them were noted. **Results and conclusion:** The popular guidelines on type 2 diabetes mellitus were critically reviewed and the principal points of each of the guidelines are explained along with the areas of divergence among all the guidelines.

Key words: Type 2 diabetes mellitus, Guidelines of diabetes, ADA-EASD position statement, AACE

GLOBAL BURDEN OF DIABETES

Briefly, 415 million (age group in between 20 and 79 years) people are living with diabetes worldwide with prevalence of 8.8%. In total, 77% of people with diabetes live in low and middle income countries. According to International Diabetes Federation by 2040, the expected number of population with disease burden will be 642 million. In India, in 2015 total number of people with diabetes (age between 20 and 79 years) was 69.2 million and expected to increase to 123.5 million by 2040. In South East Asia, the number of people with diabetes mellitus is 78 million and death because of diabetes is 1.2 million.[1] Evidence based clinical guidelines are often regarded as the best tools for the management of any chronic disease like type 2 diabetes mellitus and thus provide a benchmark to achieve optimal patient outcome. There are various recommendations currently followed in different parts of the world issued by various international and national bodies or professional organizations as to management of type 2 diabetes mellitus and/or its complications. These include guidelines from the American Diabetes Association (ADA), the European Association for the Study of Diabetes (EASD), the World Health Organisation (WHO), the American Association of Clinical endocrinologists (AACE), International Diabetes Federation (IDF), etc. Others like

Indian Council of Medical Research (ICMR), the Indian Health Service (IHS) have also issued management guidelines from time to time. Of them, the AACE document is a series of algorithms with very minimal text which mainly deals with all facets of type 2 diabetes, i.e., hyperglycemia, obesity, pre-diabetes, hypertension, and dyslipidemia. Whereas the ADA/the present study focuses mainly on comparing various type 2 diabetes management protocols and guidelines currently in practice by diabetologists in a diverse geographical areas. Undoubtedly local incidence and disease patterns influence the respective guidelines, still considering the fact that type 2 diabetes mellitus is now considered as a modern day epidemic, this article reviews the similarities and deviations amongst various existent guidelines.

CURRENT TRENDS IN THE MANAGEMENT OF TYPE 2 DIABETES MELLITUS

AACE (American Association of Clinical Endocrinologist) principles of management of type 2 diabetes mellitus[2]

(1) Lifestyle optimization and education are essential for all patients with diabetes. Lifestyle modification designed for weight loss, including medical and surgical interventions

approved for the treatment of obesity, should be considered as primary approaches for therapeutic benefits in overweight and obese patients with diabetes, and for prevention of diabetes, and for prevention of diabetes in high risk patients with prediabetes. The treatment of overweight/obesity in patients with type 2 diabetes and prediabetes should proceed according to the Obesity Treatment Algorithm. Effective interventions for weight loss involve a multidisciplinary team. The need for medical therapy for weight loss or glycemic control should not be considered as a failure of lifestyle management, but as an adjunct to it.

(2) The HbA1c target must be individualized, based on numerous factors, such as age, comorbid conditions, duration of diabetes, risk of hypoglycemia, patient motivation, adherence, life expectancy, etc. An HbA1c of 6.5% or less is still considered optimal if it can be achieved in a safe and affordable manner, but higher targets may be appropriate and may change in a given individual over time.

(3) Minimizing risk of hypoglycemia is a priority. It is a matter of safety, adherence, and cost.

(4) Glycemic control targets include fasting and post-prandial glucose as determined by self-blood glucose monitoring.

(5) Minimizing risk of weight gain is a priority and is a matter of safety, adherence, and cost.

(6) The choice of therapies must be individualized based on attributes of the patient (as above) and the medications themselves. Attributes of medications that affect their choice include risk of inducing hypoglycemia, risk of weight gain, and ease of use, cost and safety impact of kidney, heart, or liver disease. This algorithm also stratifies choice of therapies based on initial HbA1c.

(7) The algorithm provides guidance to what therapies to initiate and add, but respects individual circumstances that would make different choices.

(8) Therapies with complementary mechanisms of action must typically be used in combinations for optimum glycemic control.

(9) Effectiveness of therapy must be evaluated frequently until stable (e.g., every 3 months) using multiple criteria including HbA1c, SMBG (self-monitoring of blood glucose) records including both fasting and postprandial data, documented and suspected hypoglycemia, and monitoring for other potential adverse events (weight gain, fluid retention, hepatic, renal, or cardiac disease) and monitoring of comorbidities, relevant laboratory data, concomitant drug administration, diabetic complications, and psychosocial factors affecting patient care.

(10) Safety and efficacy should be given higher priorities than initial acquisition cost of medications per se since cost of medication is only a small part of the total cost of a medication, consideration should be given to monitoring requirements, risk of hypoglycemia, weight gain, etc.

(11) The algorithm should be as simple as possible to gain physician acceptance and improve its utility and usability in clinical practice.

(12) The algorithm should serve to help educate the clinician as well as to guide therapy at the point of care.

(13) The algorithm should conform as nearly as possible to a consensus for current standard of practice of care by expert endocrinologists who specialize in the management of patients with type 2 diabetes and have the broadest experience in outpatient clinical practice.

(14) The algorithm should be as specific as possible, and provide guidance to the physician with prioritization and a rationale for selection of any particular regimen.

(15) Rapid acting insulin analogues are superior to NPH insulin because they provide a fairly flat response for approximately 24 h and provide better reproducibility and consistency both between subjects and within subjects with a corresponding reduction in the risk of hypoglycemia.

Standards of Medical Care in Diabetes – 2016 (American Diabetic Association) and European Association for the Study of Diabetes (EASD) Position Statement

1) **Strategies for Improving Care**
   a) A patient centered communication style that incorporates patient preferences, assesses literacy and numeracy, and addresses cultural barriers to care should be used.
   b) Treatment decisions should be timely and founded on evidence based guidelines that are tailored to individual patient preferences, prognosis, and comorbidities.
   c) Care should be aligned with components of the Chronic Care Model (CCM) to ensure productive interactions between a prepared proactive practice team and an informed activated patient.
   d) When feasible, care systems should support team-based care, community involvement, patient registries, and decision support tools to meet patient needs.
   e) People with diabetes should receive medical care from a collaborative, integrated team with expertise in diabetes. This team may include physicians, nurse practitioners, physicians' assistants, nurses, dieticians, pharmacists, and mental health professionals.

2) **Diabetes Management**
   Glycemic recommendations for non-pregnant adults with diabetes
   (i) HbA1c < 7.0 %
       Pre-prandial capillary plasma glucose 80–130 mg/dl.
       Postprandial capillary plasma glucose < 180 mg/dl.
       a) Less stringent goals (such as < 8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular, or macrovascular complications, extensive comorbid conditions, or long standing diabetes in whom the general goal is difficult to attain despite diabetes self-management education, appropriate self-management education, appropriate glucose monitoring, and effective doses of multiple glucose lowering agent including insulin.

b) Providers might reasonably suggest more stringent HbA1C goals (such as < 6.5%) for selected individual patients if this can be achieved without significant hypoglycemia or other adverse effect of treatment. Appropriate patients might include those with short duration of diabetes, type 2 diabetes treated with lifestyle or metformin only, long life expectancy, or no significant cardiovascular disease.

c) Lifestyle modification
   1. Diabetes self-management education and self-management support.
   2. Medical Nutrition Therapy – Individualized medical nutrition therapy. Meal planning from a registered dietician. Comprehensive group diabetes education programs including nutrition therapy or individualized education sessions have reported HbA1C decreases of 0.3–1% for type 1 diabetes[3–7] and 0.5–2% for type 2 diabetes.[8–15]

(ii) Carbohydrate management
A simple diabetes meal planning approach such as portion control or healthful food choices may be better suited for individuals.[16–19] Carbohydrate intakes from vegetables, fruits, whole grains, legumes, and dairy products should be advised over intake from other carbohydrate sources, especially those that contain added fats, sugars, or sodium. Individuals at high risk for type 2 diabetes should consume foods containing whole grains.

(iii) Protein management
Mediterranean style eating pattern, rich in monounsaturated fatty acids is appropriate for type 2 diabetes mellitus.

(iv) Dietary fat managementIncreased consumption of foods containing long chain omega-3 fatty acids, such as fatty fish, and omega-3-linolenic acid (ALA) is recommended.
The consumption of fish (particularly fatty fish) at least two times per week is recommended.

(v) Physical activity
   a) Children with diabetes or pre-diabetes should be encouraged to engage in at least 60 min of physical activity each day.
   b) Adults with diabetes should be advised to perform at least 150 min/week of moderate intensity aerobic physical activity (50–70% of maximum heart rate), spread over at least 3 days/week with no more than 2 consecutive days without exercise.
   c) Evidence supports that all individuals, including those with diabetes, should be encouraged to reduce sedentary time, particularly by breaking up extended amounts of time (> 90 min) spent sitting.
   d) In the absence of contraindications, adults with type 2 diabetes should be encouraged to perform resistance training at least twice per week.
   e) High risk patients should be encouraged to start with short periods of low intensity exercise and slow slowly increase the intensity and duration.
   f) In individuals taking insulin or insulin secretogogues, physical activity can cause hypoglycemia if medication dose or carbohydrate consumption is not altered. For individuals on these therapies, added carbohydrate should be ingested if pre-exercise glucose levels are < 100 mg/dl.

(vi) Smoking cessation
   a) Patients should not smoke or use tobacco products.
   b) Smoking cessation counselling and other forms of treatment as a routine component of diabetes care.

(vi) Psychosocial assessment and care
   a) Stepwise collaborative care approach for the management of depression.
   b) Older adults (≥ 65 years) with diabetes should be considered a high priority population for depression screening and treatment.
   c) Screen for psychosocial problems such as depression, diabetes-related distress, anxiety, eating disorders, and cognitive impairment.
   d) Include assessment of the patient's psychological and social situation as an ongoing part of the medical management of diabetes.

(vii) Immunization
   a) Routine vaccination for children and adults with diabetes as for the general population.
   b) Annually provide an influenza vaccine to all patients with diabetes ≥ 6 months of age.
   c) Administer pneumococcal polysaccharide vaccine 23 (PPSV23) to all patients with diabetes ≥ 2 years of age.
   d) Administer hepatitis B vaccination to unvaccinated adults with diabetes who are aged 19–59 years.
   e) Consider administering hepatitis B vaccination to unvaccinated adults with diabetes who are aged ≥ 60 years.

Pharmacological Therapy for Type 2 Diabetes

a) Metformin if not contraindicated and if tolerated, is the preferred initial pharmacological agent for type 2 diabetes.

b) If noninsulin monotherapy at maximum tolerated dose does not achieve or maintain the HbA1C target over 3 months, add a second oral agent, a GLP-1 receptor agonist, or basal insulin.

c) Due to the progressive nature of type 2 diabetes, insulin therapy is eventually indicated for many patients with type 2 diabetes.

d) In patients with newly diagnosed type 2 diabetes and markedly symptomatic and or elevated blood glucose levels or HbA1C, consider initiating insulin therapy.

e) A patient-centered approach should be used to guide choice of pharmacological agents. Considerations include efficacy, cost, potential side effects, weight, comorbidities, hypoglycemia risk, and patient preferences.

f) Most patients should begin with lifestyle changes (life style counselling, weight loss education, exercise, etc.). When lifestyle efforts alone have not achieved or maintained glycemic goals, metformin monotherapy should be added at, or soon after diagnosis unless there are contraindications or intolerance.

g) Metformin has a long standing evidence base for efficacy and safety, is inexpensive and may reduce risk of cardiovascular events.[20]

h) In patients with metformin intolerance or contraindications, consider an initial drug from other classes like sulfonylurea or thiazolidinedione or DPP-4 inhibitor or GLP1 receptor agonist or basal insulin.

i) If the HbA1ctarget is not achieved after approximately 3 months, consider a combination of metformin and one of the six treatment options: sulfonylurea, thiazolidinedione, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, basal insulin.

j) Drug choice is based on patient preferences as well as various patient, disease, and drug characteristics, with the goal of reducing blood glucose levels while minimizing side effects, especially hypoglycemia.

k) Rapid acting secretogogues (meglitinides) may be used instead of sulfonylureas in patients with irregular meal schedules or who develop late postprandial hypoglycemia on a sulfonylurea.

l) For all patients, consider initiating therapy with a dual combination when HbA1c is ≥ 9% to more expeditiously achieve target HbA1c level.

m) Insulin has the advantage of being effective where other agents may not be and should be considered as part of any combination regimen when hyperglycemia is severe, especially if symptoms are present or any catabolic features (weight loss, ketosis) are in evidence.

n) Consider initiating combination insulin injectable therapy when blood glucose is ≥ 300–350 mg/dl and/or HbA1c is ≥ 10–12%.

Insulin Therapy

a) Basal insulin alone is the most convenient initial insulin regimen, beginning at 10 IU or 0.1–0.2 U/kg, depending on the degree of hyperglycemia.

b) Basal insulin is usually prescribed in conjunction with metformin and possibly one additional noninsulin agent.

c) If basal insulin has been titrated to an acceptable fasting blood glucose level, but HbA1C remains above target, consider advancing to injectable therapy to cover postprandial glucose excursions.

Bariatric Surgery

1) Bariatric surgery may be considered for adults with Body Mass Index (BMI) > 35 kg/m^2 and type 2 diabetes, especially if diabetes or associated comorbidities are difficult to control with lifestyle and pharmacological therapy.

2) Patients with type 2 diabetes who have undergone bariatric surgery need lifelong lifestyle support and medical monitoring.

Cardiovascular Disease Risk Management

A) Hypertension and blood pressure control
Blood pressure should be measured at every routine visit. Patients found to have elevated blood pressure confirmed on a separate day.

Goals

a) People with diabetes and hypertension should be treated to a systolic blood pressure (SBP) goal of < 140 mm of Hg.

b) Individuals with diabetes should be treated to a diastolic blood pressure (DBP) < 90 mm of Hg.

c) Lower diastolic targets, such as < 80 mm of Hg, may be appropriate for certain individuals, such as younger patients, if they can be achieved without undue treatment burden.

d) Lower systolic targets, such as < 130 mm of Hg, may be appropriate for certain individuals, such as younger patients, if they can be achieved without undue treatment burden.

B) Dyslipidemia management

a) Lifestyle modification focusing on the reduction of saturated fat, trans fat, and cholesterol intake, increase of omega-3-fatty acids, viscous fiber, and plant sterols/stools; and increased physical activity should be recommended to improve the lipid profile in patients with diabetes.

b) Intensify lifestyle therapy and optimize glycemic control for patients with elevated triglyceride levels (≥ 150 mg/dl) and or low HDL cholesterol (< 40 mg/dl for men, < 50 mg/dl for women).

c) For patients with fasting triglyceride levels ≥ 500 mg/dl evaluate for secondary causes and consider medical therapy to reduce risk of pancreatitis.

d) For patients of all ages with diabetes and overt cardiovascular disease (CVD) high intensity statin therapy should be added to lifestyle therapy.

e) For patients with diabetes aged < 40 years with additional CVD risk factors, consider using moderate or high intensity statin and lifestyle therapy.

f) For all patients with diabetes aged 40–75 years or above with or without additional CVD risk factors, consider using high or moderate intensity statin and lifestyle therapy.

g) Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of CVD.

h) Consider aspirin therapy (75–162 mg/day) as a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10-year risk > 10%). This includes most men aged > 50 years or women aged > 60 years who have at least one additional major risk factor (family history of CVD, hypertension, smoking, dyslipidemia or albuminuria).

C) Coronary heart disease

a) In patients with known CVD, use aspirin and statin therapy if not contraindicated and consider ACE inhibitor therapy to reduce the risk of cardiovascular events.

b) In patients with MI, β blockers should be continued at least 2 years after the event.
c) In patients with symptomatic heart failure, thiazolidinedione treatment should not be used.
d) In patients with stable CHF, metformin may be used if renal function is normal but should be avoided in unstable or hospitalized patients with CHF.

Diabetic nephropathy

a) Either an ACE inhibitor or ARB is suggested for the treatment of the non-pregnant patient with modestly elevated urinary albumin excretion (30–299 mg/day) and is recommended for those with urinary albumin excretion > 300 mg/day.
b) An ACE inhibitor or ARB is not recommended for the primary prevention of diabetic kidney disease in patients with diabetes who have normal blood pressure and normal UACR (< 30 mg/g).

Diabetic retinopathy

a) Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes.
b) Optimize glycemic control and blood pressure control.

Diabetic neuropathy

a) All patients should be screened for diabetic peripheral neuropathy (DPN) starting at diagnosis of type 2 diabetes and at least annually thereafter using simple clinical tests like 10 g monofilament.
b) Tight glycemic control to slow down progression of diabetic neuropathy.
c) Drugs like pregabaline, duloxetine, tapentadol, venlafexine, amitriptyline, gabapentine, valproate, and other opioids like morphine may be effective.

International Diabetes Federation Global Guidelines for Type 2 Diabetes Mellitus

Healthcare provided by International Diabetes Federation (IDF) has been divided into 3 types.

1. *Recommended care* – Cost-effective evidence-based health care.
2. *Limited care* – Healthcare for limited resources system.
3. *Comprehensive care* – Most up to date technology-based healthcare but some of the technologies are weak evidence based.

Diagnosis for Diabetes

Diagnosed as any one of the following criteria of WHO-FBG > 126 mg/dl or 75 mg OGTT test FBG > 126 mg/dl and or 2 h plasma glucose > 200 mg/dl.

Random blood glucose > 200 mg/dl with management of type 2 DM

Management of Type 2 DM

A. Education
Patient-centered structured self-management education.

Appropriately trained multidisciplinary team if possible include family member in that team.
Education should be accessible to all population including culture, ethnicity, and psychosocial issue.
B) Psychological care
Refer to a mental healthcare professional if severe coping problem, major depression, anxiety disorder, personality disorder, cognitive decline occurs.
C) Lifestyle modification
a) Physical activity 30–40 min/day for 3–5 days per week or an accumulation of 150 min per week of moderate intensity exercise.
b) Reduce food which has high energy, added sugar, and alcohol.
c) Advice on food for prevention of management of hypoglycemia.
d) Nutritional counselling from professional nutritionist.

Glucose control levels

HbA1c < 7%
Primeval capillary plasma glucose < 115 mg/ dl
Postmeal capillary plasma glucose < 160 mg/ dl

Clinical monitoring

a) Measure HbA1c at every 2–6 month interval.
b) If HbA1c not available measure fructose amine or blood glucose.
c) HbA1c should be measured by high-performance liquid chromatography or mass spectrometry.

Self-monitoring of blood glucose

a) Self-monitoring of blood glucose should be done by making the patient knowledgeable on diabetes.
b) Patient has to make willing and cooperative on self-monitoring.
c) Both the healthcare provider and receiver should agree on self-monitoring of blood glucose.

Glucose control therapy

A) First line of therapy
Metformin should be the first line of drug until and unless any other contraindications or renal impairment occurs.
Titrate the dose of metformin to counter gastrointestinal intolerance.
Monitor renal function and use metformin with caution if eGFR (estimated glomerular filtration rate) < 45 ml/min/1.73 m^2.
Sulfonylurea can be added if high blood glucose level in some population and also alpha glucosidase inhibitor can be added.
In some conditions dual therapy can be started if monotherapy cannot maintain target blood glucose level.
B) Second line of therapy
Sulfonylurea should be added as 2nd line therapy.
Other options may be metformin if not added as first line of therapy.
Alpha glucosidase inhibitor or DPP4 inhibitor or thiazolidinedione can be added.

C) Third line of therapy
Add oral antidiabetic agent or start insulin.
If starting with insulin add premixed or basal insulin.
Add alpha glucosidase inhibitor or DPP4 inhibitor or thiazolidinedione.
Other option may be glucagon like peptide receptor agonist.

D) Fourth line of therapy
Begin with insulin therapy when lifestyle modification and oral antidiabetic medication could not control optimum blood glucose level.

Insulin Therapy

Begin with basal insulin like Insulin detemir or Insulin glargine
Or
Once or twice daily premixed insulin
Initiate insulin with a self-titration regimen (dose increases by 2 units by every 3 days) or with biweekly or more frequently by contacting with a healthcare professional.
Premeal glucose target should be < 115 mg/dl.
Explain that initial insulin level below but eventually insulin requirement may vary 30–100 units/day.
Other oral antidiabetic medication may be continued.

Comparative evaluation of recent guidelines on type 2 diabetes mellitus management

Comparison of screening guidelines

The WHO, ADA-EASD position statement, and IHS guidelines state that adult people should be screened for type 2 diabetes if their BMI >25 kg/m^2 and have one or more of the following risk factors: first degree relative with diabetes, women who delivered a baby weighing > 9 lb, diagnosis of polycystic ovarian syndrome, history of gestational diabetes mellitus (GDM), or acanthosis nigricans.[20–22] Although the basic guidelines remain the same, there are some differences in individual guidelines. The WHO recommends that adults having history of vascular disease to be screened every 3 years. The recommendation of ADA-EASD position statement also mentions that adults with age more than 45 years without any pre-existing conditions be screened every 3 years. The ADA-EASD position statement also recommends annual screening of pre-diabetic adults. However, the AACE guideline[23] has done away with the criterion of having a BMI >25 kg/m^2 in adults for diabetes screening. On the other hand, the AACE guideline has recommended that those adults having impaired glucose tolerance (IGT), or having a history of cardiovascular disease, physical inactivity, or are on antipsychotic therapy for schizophrenia or severe bipolar disorder; should only undergo screening tests for the presence of diabetes.[23] Another important screening criteria included in all the guidelines are the presence of HDL cholesterol <35 mg/dl or triglyceride level >250 mg/dl. Both the WHO and the ADA-EASD guidelines recommend that in the event of a normal screening test values, they should be repeated every 3 years.[24]

Comparison of diagnosis guidelines

Almost all the guidelines are in unison as to the diagnostic criteria for type 2 diabetes mellitus. For non-pregnant adults, the diagnosis of diabetes mellitus is made if there is fasting plasma glucose (FPG) level ≥ 126 mg/dl or 2-h postprandial plasma glucose level of ≥ 200 mg/dl following a standard 75 mg oral glucose load.[20,22,23] In contrast, the WHO guideline also includes those with a random plasma glucose ≥ 200 mg/dl and having classic symptoms of hyperglycemia as a criteria for diagnosis.[21] In addition the AACE, ADA-EASD position statement, and IHS also recommend that a person having HbA1c > 6.5% can also be diagnosed as having diabetes.[25]

Comparison of Guidelines for management

All the patients diagnosed with type 2 diabetes mellitus require elaborate and well-planned long-term management strategies. Diabetes self-management education and also medical nutrition therapy are considered the most effective early management strategies for type 2 diabetes. Proper education about the various facets of diabetes and self-management goes a long way towards helping the patients adhere to a long-term treatment process, achieving favorable glycemic control and weight reduction.[24] All the guidelines including the WHO, ADA-EASD, AACE are in agreement to recognize the importance of medical nutrition therapy and diabetes self-management education in management of type 2 diabetes.[20–23,25] Amongst all this, the ADA-EASD position statement guidelines recommend use of metformin as the first line drug in patients in whom it is not contraindicated due to some other reason.[20] However, the AACE guidelines recommend, instead of prioritizing a single medicine, a host of other drugs any of which may be started either alone or in combination depending on the initial HbA1c percentage.[25] Regarding HbA1c as a glycemic goal, the ADA-EASD position statement and the WHO guidelines have recommended an HbA1c < 7% in all type 2 diabetes patients.[20,21] However, in the recent 2016 guidelines of the ADA-EASD position statement, more stringent HbA1c goals like < 6.5% or even less stringent HbA1c goals such as < 8% may be considered based on individualized patient profile.[20] On the other hand, the AACE has recommended for an individualized goal of HbA1c as to < 6.5% for patients without severe illness and at low hypoglycemic risk, whereas for elder patients with concurrent serious illness and at risk for hypoglycemia, the goal may be even > 6.5%.[23,25] The ADA-EASD, AACE, and IHS also recommend HbA1c testing twice yearly or four times yearly for patients not at target.[20,22,23,25] Apart from glycemic management, there are also several subtle differences between different guidelines regarding management of other comorbidities that are frequently present in type 2 diabetic patients. The ADA-EASD position statement, WHO and AACE guidelines recommend initiation of aspirin (preferably in low dose) in diabetic patients having cardiovascular risk factors, more so in males having age > 50 years and females having age > 60 years.[20–23,25] With regard to lipid lowering therapy, the ADA-EASD, AACE, and IHS recommend initiation of statins

regardless of baseline levels unless contraindicated,[20,22,23,25] while the WHO guidelines only recommend starting statins if LDL-C level is high.[21] Daily foot care is given due importance in the ADA-EASD, AACE, and IHS guidelines except in WHO guidelines.[20–22] However, unlike the ADA-EASD position statement, the AACE guidelines do not lay any emphasis on annual comprehensive foot examinations.[23,25] Several micro- and macrovascular complications associated with diabetes markedly reduce the quality of life in patients. All the guidelines recommend yearly eye examination to be performed for screening retinopathy.[20–23,25] To identify and diagnose the diabetic nephropathy, another serious complication of long standing diabetic patients, annual testing of serum creatinine and urine albumin are recommended by all the guidelines.[20–23,25] The ADA-EASD and IHS guidelines also recommend screening for distal symmetric polyneuropathy at diagnosis and yearly thereafter.[20,22] Regarding alcohol intake in type 2 diabetics, only the ADA-EASD and IHS recommend to limit alcohol intake to a moderate amount (≤1 drink/day for women and ≤ 2 drinks/day for men).[20,22] The ADA-EASD position statement also recommends assessing for few common diabetes-associated conditions like hearing impairment, obstructive sleep apnea, fatty liver disease, low testosterone in men, periodontal disease, cancers (liver, pancreas, endometrium, colon/rectum, breast, and bladder), fractures, cognitive impairment.[20] In contrast, the AACE only recommends screening for obstructive sleep apnea in men > 50 years of age and regular assessment for diabetes associated depression.[23,25] Regarding management of hyperlipidemia, all the guidelines are generally in consensus that goals for lipids should be as follows: LDL-C < 100 mg/dl in patients without overt CVD; LDL-C < 70 mg/dl in patients with overt CVD; HDL-C > 40 mg/dl in men, and > 50 mg/dl in women; and a triglyceride level of < 150 mg/dl.[20–25] Regarding medical management of prediabetes, the use of metformin therapy differs in the ADA and AACE guidelines. As per ADA-EASD position statement, metformin should be prescribed for patients with IGT, IFG, or and HbA1c of 5.7–6.4%; a BMI > 35 kg/m^2, age < 60 years, or (for women) previous history of gestational diabetes mellitus.[20,24] Whereas as per the AACE guidelines, either metformin or a thiazolidinedione can be prescribed for younger patients who are at moderate to high risk for developing diabetes; patients with additional risk factors like hypertension, dyslipidemia, or polycystic ovarian syndrome; patients with a family history of diabetes in a first degree relative, and in obese persons. The ADA-EASD and IHS guidelines also recommend annual influenza vaccine for diabetic patients.[20,22]

CONCLUSION

The present review of the various popular guidelines for the management of type 2 diabetes mellitus summarizes the basic aspects of screening, diagnosis, management, and treatment of associated comorbid diseases. All the guidelines are quite well accepted in various parts of the world, however from a physician's point of view it is very important to note the areas where there are certain disagreements among these guidelines. Although management of type 2 diabetes mellitus requires individualized patient-centric approach, yet it is of utmost importance to keep in mind the basics of the guidelines and follow a holistic approach towards achieving successful treatment outcome.

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