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Review Article

DIABETES MELLITUS: SCREENING AND DIAGNOSIS

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Abstract:

Introduction: The term 'diabetes mellitus' refers to a wide range of metabolic conditions where there is an abnormal increase of glucose levels in the blood that results from dysfunctional insulin secretion and/or activity. Recent reports estimate that within the next twenty years, the US will have more than forty-four million patients diagnosed with diabetes mellitus type 2, which is almost double the current number of diabetic patients. Generally, any individual should be suspected to have diabetes mellitus type 2 if they have an indicative history. These patients most immediately undergo the necessary work up to confirm or exclude the disease. **Aim of work:** In this review, we will discuss the most recent evidence regarding diabetes mellitus screening, diagnosis in family medicine settings. **Methodology:** We did a systematic search for diabetes mellitus screening and diagnosis in the emergency department using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles

Conclusions: Diabetes mellitus covers a wide range of metabolic conditions where abnormal glucose metabolism is present. It is considered to be the most common condition diagnosed by primary practitioners. Poor control on diabetes mellitus, regardless of the subtype, will lead to the development of severe complications in different body organs like loss of sight, amputation of extremities, chronic kidney disease and renal failure, vasculopathies, and cardiovascular diseases. In this review we discussed proper screening methods for each subgroup. Once an abnormal finding is detected during screening methods, further evaluation is required to confirm or exclude the presence of diabetes. Studies have found that screening for diabetes was associated with improved overall 30-year survival in most subgroups.

Key words: Diabetes mellitus, screening, diagnosis, management.

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INTRODUCTION:

The term 'diabetes mellitus' refers to a wide range of metabolic conditions where there is an abnormal increase of glucose levels in the blood that results from dysfunctional insulin secretion and/or activity [1,2]. Lack of proper control of glucose levels in the blood in diabetic patients can lead to the development of several severe long-term complications in different body organs like loss of sight, amputation of extremities, chronic kidney disease and renal failure, vasculopathies, and cardiovascular diseases. Recent reports estimate that within the next twenty years, the US will have more than forty-four million patients diagnosed with diabetes mellitus type 2, which is almost double the current number of diabetic patients. Moreover, the incidence and prevalence of diabetes will continue to further increase to become the most commonly diagnosed disease by primary care providers [3].

Generally, any individual should be suspected to have diabetes mellitus type 2 if they have an indicative history. These patients most immediately undergo the necessary work up to confirm or exclude the disease. Clinical manifestations that usually raise the suspicion for the presence of diabetes include increased urination, increased thirst, general fatigue, decreased visual acuity and the presence of blurring, loss of weight, delayed healing of wounds, and numbness sensation.

In this review, we will discuss the most recent evidence regarding diabetes mellitus screening, diagnosis in family medicine settings.

METHODOLOGY:

We did a systematic search for diabetes mellitus screening and diagnosis in the emergency department using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: diabetes mellitus, screening, diagnosis, family medicine,

Classifying Diabetes

Diabetes mellitus generally has two main types: type 1 and type 2. Type 1 results from the destruction of pancreatic beta-cells due to autoimmune reactions, and usually starts during childhood. Type 2, on the other hand, is a result of the development of insulin insensitivity, and generally occurs in overweight and obese individuals [2]. Diabetes mellitus was previously a disease of adults. However, incidence of

diabetes mellitus type 2 has been significantly increasing among obese adolescents and even children. Similar long-term complications and comorbidities on different body organs occur following both types of diabetes.

TYPE 1 DIABETES Screening:

All guidelines do not recommend the screening for diabetes mellitus type 1. Reasons behind this include [4]:

- Most patients with diabetes mellitus type 1 will develop the disease acutely, making it not possible to detect the disease earlier than the appearance of symptoms.
- No solid evidence is present on the threshold of diabetes mellitus type 1 antibody levels, above which a diagnosis can be made.
- Asymptomatic patients with diabetes mellitus type 1 are not indicated to receive any treatment, and treatment of the disease is only symptomatic.
- Even if early disease is detected, or predisposed individuals are identified, no intervention is present to prevent the progression of the condition.

TYPE 2 DIABETES Screening:

On the contrary, screening for diabetes mellitus type 2 is highly recommended to be performed by family doctors and primary care providers. Reasons behind this include [5].

- Many reliable tests are present to early diagnose the disease and detect prediabetic patients before the progress into diabetes.
- When diabetes is early detected, the application of lifestyle modifications and the use of pharmacological agents can prevent the progression of the disease and decrease rates of diabetes in prediabetic patients.
- Even in patients who finally progress to diabetes, early interventions decrease the rate and severity of long-term complications associated with the disease.
- Asymptomatic prediabetics can significantly benefit from early interventions.

Despite all these proposed benefits of screening for diabetes mellitus type 2, some studies have found that the overall 10-year survival does not significantly differ or improve following the application of screening [6].

Most studies have concluded that the proper application of lifestyle modifications along with pharmacological interventions will significantly

delay, or even prevent, the development diabetes mellitus type 2 in prediabetic individuals with impaired fasting glucose or glucose intolerance.⁷ Some studies have suggested that lifestyle modifications are even superior to pharmacological interventions in preventing or delaying diabetes mellitus type 2 [7].

Some studies have recommended early screening for diabetes as they found it was associated with better overall 30-year survival.⁸ In a previous clinical trial, both overall 23-year survival and cardiovascular-specific 23-year survival were significantly improved among patients with glucose intolerance, following the application of lifestyle modifications. However, these results were found in a Chinese population and, thus, may not be able to be generalized for other populations around the world [9].

In addition to lifestyle modifications, and pharmacological interventions, the ADA recommended in their latest statement the importance of psychosocial assessment and interventions in prediabetic patients, as this could improve the progression of their condition. Therefore, some tools have been created to assess these aspects among prediabetic and diabetic patients. In addition to maintaining psychosocial health, recent guidelines also focus on decreasing the disparities among different populations regarding screening for diabetes and its prevention. To achieve this, these guidelines recommend the use of the Chronic Care Model that integrates the patients in the decision making, management, and treatment, along with including a multi-disciplinary team that will follow the patients and ensure the application of best interventions.

Who Should Be Screened?

Nonpregnant Adults:

Many guidelines have recently published their recommendations to the screening for diabetes mellitus type 2 among different subpopulations [10]. Guidelines published by the US Preventive Service Task Force recommend that any individual between forty to seventy years with a body mass index that is higher than 25 must be screened for the presence of diabetes mellitus type 2. Any individual found to have abnormal findings on screening test should undergo further evaluation by experts, and start applying intense lifestyle modifications that must include higher physical activity and modified more healthy diet. Individuals with higher risk must start screening at earlier ages to detect diabetic status as early as possible. These guidelines are based on large

trials that studied screening for diabetes and its effects on survival and mortality in different subpopulations.

The American Diabetes Association, on the other hand, has different guidelines where they recommend broader screening for diabetes mellitus type 2. In their latest guidelines, they recommended the initiation of screening for prediabetes and diabetes mellitus type 2 in any individual who is older than forty-five years, without considering the presence of other predisposing factors or cardiovascular risks.¹¹

The risk of developing diabetes mellitus type 2 among any individual can be estimated using different calculators [12]. However, many authors claim that these calculators may overestimate the risk of developing diabetes mellitus type 2. The Canadian Task Force on Preventive Health Care has recommended the use of their validated questionnaires to predict the risk of developing diabetes mellitus type 2 and determine individuals who must be screened before developing the disease. It is also important that any individual who is prediabetic or considered high-risk, must be annually screened for the development of diabetes mellitus type 2. While individuals with less risk could undergo screening once every 3 years [13].

PREGNANT WOMEN:

Having abnormal glucose levels in blood can significantly harm the fetus by increasing the risks of developing congenital malformations, and possibly leading to intrauterine death. Moreover, pregnant females who receive a diagnosis of gestational diabetes mellitus and are found to have abnormal fasting glucose levels, are at a significantly higher risk of delivering a baby with anatomical malformations [14].

Screening of pregnant females for the presence of diabetes or prediabetes aims at the reduction of both maternal complications and fetal complications, which can be severe or even fatal, and include the development of preeclampsia/eclampsia, the need for cesarean delivery, developing congenital malformations, increased fetal weight, childhood obesity, dystocia of the shoulder, palsy of multiple nerves, pathological fractures, congenital jaundice, and idiopathic infant death [15].

According to the American Diabetes Association, all pregnant females should be screened for the presence

of diabetes mellitus type 2 or gestational diabetes mellitus during their first trimester of pregnancy, especially if they already have predisposing factors for diabetes. Females with higher needs for screening include obese females, older females, the presence of a prior pregnancy with gestational diabetes, and having a positive family history of diabetes mellitus type 2 or gestational diabetes. ¹⁷ Both the CDC and the American College of Obstetricians and Gynecologists have similar recommendations for the screening for diabetes in pregnant females. However, the USPTF have slightly different recommendations, as they recommend screening for the same groups of patients but at the 24th week of pregnancy rather than the first trimester [16].

Screening for diabetes mellitus type 2 and gestational diabetes in pregnant females generally follows a 2-step approach of a glucose challenge test. First a 50 g dose of glucose is administered. If results come back positive, a diagnostic second dose of 100 g glucose is administered [16].

CHILDREN

Based on the guidelines published by the American Diabetes Association, adolescents, or even children, may be required to undergo screening for diabetes mellitus type 2 if they have high body mass index that is higher than the 85th percentile for their sex and age. In addition, a child whose weight that is 120% more than the proper weight for age. Having a positive family history of diabetes mellitus types 2 also make it important to screen children for diabetes. Other factors that indicate screening for diabetes mellitus type 2 in children include the presence of acanthosis nigricans, high blood pressure, dyslipidemia, and polycystic ovary syndrome (in females). For any child or adolescent with the previously mentioned predisposing factors, screening is recommended every 2 years starting from puberty or ten years of age, whichever comes first [17].

OLDER ADULTS:

Large populations-based studies suggest that about half adults are prediabetics, with a significantly high risk of developing diabetes mellitus type 2. However, benefits of screening generally depend on the general status of the patient, the presence of other chronic comorbidities, and the availability of medical interventions that will improve the disease in these patients. Generally, screening for diabetes mellitus type 2 in the elderly populations has been found to improve overall survival on the long-term [18].

Currently, all guidelines do not recommend the screening for diabetes mellitus type 2 in extremely old patients, except when individuals are susceptible for the development of diabetes-related long-term complications. When screening is applied in this subpopulation, thresholds for diagnosis are similar to the general population. However, treatment and management plans are significantly different due to the different goals of management. ¹⁹ No guidelines have set an age when screening must not be performed anymore. Therefore, the decision to stop diabetes screening should be made by both the clinician and the elderly individual, based in several factors including life expectancy and the presence of other diseases.

Diagnostic Testing following positive screening tests:

In any individual who undergoes screening tests for diabetes mellitus type 2, and receives positive results, further evaluation and work up must be performed to confirm or exclude the presence of the disease. Generally, a diagnosis with diabetes mellitus type 2 is made when classical clinical manifestations are present along with abnormal blood glucose levels. Glucose levels are considered abnormal if a random blood sample shows glucose higher than 200 mg/dl. In addition to random glucose testing, the levels of HbA1c can also be measured to detect the presence of long-term glucose impairments. Generally, having HbA1c levels higher than 6.5% indicate the presence of diabetes mellitus in the patient.

Other tests that can be used in suspected diabetic patients include:

- Fasting plasma glucose, which is considered diabetic when is more than 126 mg/dl (or 7 mmol/L).
- Oral glucose tolerance test, which should be repeated on two different days before reaching a diagnosis.

The use of more than one test is indicated in individuals who have results that are not consistent with the clinical picture.

A1C LEVEL

HbA1c is the percent of hemoglobin glycosylation and is used to estimate the average levels of plasma glucose over the last 3 months. ²⁰ The use of HbA1c

measurement for diagnosing and following patients with diabetes was first started in the year 2010, when the American Diabetes association recommended this in their guidelines. Since then, measurement of HbA1c has been widely used both for the detection of the disease, and for the progression of it, as it can reflect the response of the disease to treatment.

However, despite having many advantages, HbA1c is still associated with several limitations including the inability to standardize the results of the test. This is a result of the absence of a complete correlation between glucose levels and HbA1c levels in some patients. For example, patients who suffer from huge blood loss or blood hemolysis can have false negative HbA1c results. on the other hand, patients who have had splenectomy before or who suffer from aplastic anemia can have false positive HbA1c results due to the significant increase in the age of blood cells. Different changes in HbA1c results can also be observed in patients with hemoglobinopathies or any abnormality leading to hemoglobin dysfunction. Differences in HbA1c measurements can also be detected between different racial groups.²¹

Based on these previously mentioned limitations, it is not recommended to diagnose or exclude diabetes mellitus type 2 based only on HbA1c measurement, but rather perform multiple investigations before reaching a diagnosis. 2,17 HbA1c could still be used as a reliable measure of the progression of the disease after a baseline level has been set.

FASTING PLASMA GLUCOSE:

Recent published data have shown that measuring fasting glucose levels can have about 30% higher sensitivity in detecting diabetes mellitus than measuring HbA1c levels.²²fasting glucose levels can be easily measured with a single venous sample.

SPECIAL TESTS:

As we previously mentioned, the term 'diabetes mellitus' covers a wide range of diseases, mainly diabetes mellitus type 1 and diabetes mellitus type 2. Other conditions include gestational diabetes mellitus, neonatal and infantile diabetes, maturity-onset diabetes of youth, and autoimmune diabetes mellitus. Causes and etiologies of these different types may overlap in some cases.²³ After making a diagnosis of diabetes mellitus, by confirming the presence of abnormal glucose metabolism, further investigations could be used to determine the exact etiology of the disease.

Most patients with diabetes mellitus type 1 will have positive serum antibodies against pancreatic cells or any of their content. Patients with diabetes mellitus type 1 who do not have positive antibodies are termed 'idiopathic type 1'. Positive serum antibodies may also be detected in some patients with diabetes mellitus type 2 and autoimmune diabetes. Therefore, the detection of antibodies against pancreatic cells is not considered specific for diabetes mellitus type However, their use is still recommended by the American Association of Clinical Endocrinologists during the work up for diabetes mellitus type

Further studies must be conducted on the use of these tests in the workup for screening and diagnosing different subtypes of diabetes mellitus, before routinely using these tests.

CONCLUSION:

Diabetes mellitus covers a wide range of metabolic conditions where abnormal glucose metabolism is present. It is considered to be the most common condition diagnosed by primary practitioners. Poor control on diabetes mellitus, regardless of the subtype, will lead to the development of severe complications in different body organs like loss of sight, amputation of extremities, chronic kidney disease and renal failure, vasculopathies, and cardiovascular diseases. Therefore, in order to be able to prevent the development of these complications, proper treatment and management of the disease must be applied to maintain normal glucose levels. Moreover, the early detection of diabetes mellitus can have a significant impact on further complications of the disease. In addition, early detection of prediabetic status can delay or even prevent the progression into diabetes mellitus. Therefore, screening for diabetes have been recommended by many specialized organizations as it has been found to lead to significantly improved outcomes. screening for diabetes differs among different populations according to several factors: individuals characteristics, their cardiovascular risks, and the presence of other chronic comorbidities. In this review we discussed proper screening methods for each subgroup. Once an abnormal finding is detected during screening methods, further evaluation is required to confirm or exclude the presence of diabetes. Studies have found that screening for diabetes was associated with improved overall 30-year survival in most subgroups.

REFERENCES:

1. **American Diabetes Association.(2004)**

- Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2004;27(suppl 1):S5-S10.
2. **American Diabetes Association(2014)**. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014;37(suppl 1):S81-S90.
 3. **The top 20 in 2000** [Monitor]. *Fam Pract Manag*. 2002;9(5):26-29.
 4. **Patel P, Macerollo A.(2010)** Diabetes mellitus: diagnosis and screening. *Am Fam Physician*. 2010;81(7):863-870.
 5. **Selph S, Dana T, Blazina I, Bougatsos C, Patel H, Chou R.(2015)** Screening for type 2 diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2015;162(11):765-776.
 6. **Selph S, Dana T, Bougatsos C, Blazina I, Patel H, Chou R.(2008)** Screening for abnormal glucose and type 2 diabetes mellitus: a systematic review to update the 2008 U.S. Preventive Services Task Force recommendation. Rockville, Md.: Agency for Healthcare Research.
 7. **Gillies CL, Abrams KR, Lambert PC, et al.(2007)** Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ*. 2007;334(7588):299.
 8. **Gillies CL, Lambert PC, Abrams KR, et al.(2008)** Different strategies for screening and prevention of type 2 diabetes in adults: cost effectiveness analysis. *BMJ*. 2008;336(7654):1180-1185.
 9. **Li G, Zhang P, Wang J, et al.** Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study. *Lancet Diabete*.
 10. **Handelsman Y, Bloomgarden ZT, Grunberger G, et al.(2015)** American Association of Clinical Endocrinologists and American College of Endocrinology—clinical practice guidelines for developing a diabetes mellitus comprehensive care plan—2015. *Endocr Pract*. 2015;21.
 11. **Engelgau MM, Narayan KM, Herman WH.(2000)** Screening for type 2 diabetes [published correction appears in *Diabetes Care*. 2000;23(12):1868- 1869]. *Diabetes Care*. 2000;23(10):1563-1580.
 12. **Buijsse B, Simmons RK, Griffin SJ, Schulze MB.(2011)** Risk assessment tools for identifying individuals at risk of developing type 2 diabetes. *Epidemiol Rev*. 2011;33:46-62.
 13. **Takahashi O, Farmer AJ, Shimbo T, Fukui T, Glasziou PP.(2010)** A1C to detect diabetes in healthy adults: when should we recheck? *Diabetes Care*. 2010;33(9):2016-2017.
 14. **Sheffield JS, Butler-Koster EL, Casey BM, McIntire DD, Leveno KJ.(2002)** Maternal diabetes mellitus and infant malformations. *Obstet Gynecol*. 2002;100(5 pt 1):925-930.
 15. **Sacks DA, Black MH, Li X, Montoro MN, Lawrence JM.(2015)** Adverse pregnancy outcomes using the International Association of the Diabetes and Pregnancy Study Groups criteria: glycemic thresholds and associated risks. *Obstet Gynecol*. 2015;126(1):67-73.
 16. **Garrison A. Screening,(2015)** diagnosis, and management of gestational diabetes mellitus. *Am Fam Physician*. 2015;91(7):460-467.
 17. **American Diabetes Association.(2015)** (11) Children and adolescents. *Diabetes Care*. 2015;38(suppl):S70-S76.
 18. **Kirkman MS, Briscoe VJ, Clark N, et al.(2012)** Diabetes in older adults. *Diabetes Care*. 2012;35(12):2650-2664.
 19. **American Diabetes Association.(2015)** (10) Older adults. *Diabetes Care*. 2015; 38(suppl):S67-S69.
 20. **Cohen RM, Haggerty S, Herman WH.(2010)** HbA1c for the diagnosis of diabetes and prediabetes: is it time for a mid-course correction? *J Clin Endocrinol Metab*. 2010;95(12):5203-5206.
 21. **Nasir NM, Thevarajah M, Yean CY.(2010)** Hemoglobin variants detected by hemoglobin A1c (HbA1c) analysis and the effects on HbA1c measurements. *Int J Diabetes Dev Ctries*. 2010;30(2):86-90.
 22. **Picón MJ, Murri M, Muñoz A, Fernández-García JC, Gomez-Huelgas R, Tinahones FJ.(2012)** Hemoglobin A1c versus oral glucose tolerance test in postpartum diabetes screening. *Diabetes Care*. 2012;35(8):1648-1653.
 23. **Vermeulen I, Weets I, Asanghanwa M, et al.;** Belgian Diabetes Registry.