Diabetes and Cognitive Impairment: Epidemiology, Mechanisms, Treatment, and Prevention

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November 10, 2022
Presenter Disclosures

• Leonard E. Egede, MD

• Disclosed no conflict of interest
Learning Objectives

• Discuss epidemiology of diabetes
• Discuss epidemiology of cognitive impairment/dementia
• Discuss epidemiology of diabetes and cognitive impairment
• Discuss recognition and diagnosis of cognitive impairment/dementia in adults with diabetes
• Discuss potential pathways, treatment, and prevention of cognitive impairment in adults with diabetes
Case 1

- 72 year old woman with type 2 diabetes, hypertension, and hyperlipidemia
- Presents with poorly controlled diabetes and difficulty with self care
- Daughter states patient is having progressive difficulty remembering to take medications or test her sugars
- Also reports more frequent hypoglycemic episodes in past year
- Family is concerned about her safety living alone
- No recent falls, trauma, or weakness or numbness in upper/lower limbs
- A1c 11; BP 160/97; LDL 160
- Meds: NPH Insulin; Lisinopril; HCTZ; Atorvastatin
- Patient is alert; oriented to time, place, person, but admits to having more difficulty remembering to take medications or track her sugars
Question 1

• What are potential risk factors for cognitive impairment in this patient?
  A-History of hypertension and hyperlipidemia
  B-Poorly controlled diabetes
  C-Frequent hypoglycemic episodes
  D-All of the above
Question 1 - Answer

- What are potential risk factors for cognitive impairment in this patient?
  A - History of hypertension and hyperlipidemia
  B - Poorly controlled diabetes
  C - Frequent hypoglycemic episodes
  D - All of the above
Overview of diabetes
OVERVIEW OF DIABETES: PREVALENCE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Diagnosed diabetes Percentage (95% CI)</th>
<th>Undiagnosed diabetes Percentage (95% CI)</th>
<th>Total diabetes Percentage (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>10.2 (9.3–11.2)</td>
<td>2.8 (2.4–3.3)</td>
<td>13.0 (12.0–14.1)</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–44</td>
<td>3.0 (2.6–3.6)</td>
<td>1.1 (0.7–1.8)</td>
<td>4.2 (3.4–5.0)</td>
</tr>
<tr>
<td>45–64</td>
<td>13.8 (12.2–15.6)</td>
<td>3.6 (2.8–4.8)</td>
<td>17.5 (15.7–19.4)</td>
</tr>
<tr>
<td>≥65</td>
<td>21.4 (18.7–24.2)</td>
<td>5.4 (4.1–7.1)</td>
<td>26.8 (23.7–30.1)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>11.0 (9.7–12.4)</td>
<td>3.1 (2.3–4.2)</td>
<td>14.0 (12.3–15.5)</td>
</tr>
<tr>
<td>Women</td>
<td>9.5 (8.5–10.6)</td>
<td>2.5 (2.0–3.2)</td>
<td>12.0 (11.0–13.2)</td>
</tr>
</tbody>
</table>

Estimated crude prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 2013–2016

CDC, 2021
OVERVIEW OF DIABETES: TRENDS

Trends in age-adjusted prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 1999–2016.

CDC, 2021
Age-adjusted estimated prevalence of diagnosed diabetes by race/ethnicity group and sex for adults aged 18 years or older, United States, 2017–2018

CDC, 2021
### OVERVIEW OF DIABETES: ABCs

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>ABCs Goals for Many Adults</th>
<th>Less Stringent ABCs Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>&lt;7.0%</td>
<td>&lt;8.0%</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;140/90 mmHg</td>
</tr>
<tr>
<td>Cholesterol, non-HDL</td>
<td>&lt;130 mg/dL</td>
<td>&lt;160 mg/dL</td>
</tr>
<tr>
<td>Smoking, current</td>
<td>Nonsmoker</td>
<td>Nonsmoker</td>
</tr>
</tbody>
</table>

**Percentage meeting all ABCs goals**
- 19.2% met all of these criteria: A1C value <7.0%, blood pressure <140/90 mmHg, non-HDL cholesterol <130 mg/dL, and being a nonsmoker
- 36.4% met all of these criteria: A1C value <8.0%, blood pressure <140/90 mmHg, non-HDL cholesterol <160 mg/dL, and being a nonsmoker

CDC, 2021
EPIDEMIOLOGY OF DEMENTIA
PREVALENCE OF DEMENTIA

• 6.5 million individuals age 65+ living with Alzheimer’s Dementia in 2022
• Translates to 1 in 9 or 10.7% of adults 65 years or older
• 2/3 are women
• Older African Americans are 2X more likely to have AD compared to Whites
• Older Hispanics are 1.5X more likely to have AD compared to Whites

Alzheimer’s Association - https://www.alz.org/alzheimers-dementia/facts-figures
ECONOMIC BURDEN OF DEMENTIA

• Cost $321 billion in 2022
• Of that, $206 billion was cost to Medicare and Medicaid
• Projected to cost $1 trillion in 2050
• 2X higher hospital stays compared to other older adults

Alzheimer’s Association - https://www.alz.org/alzheimers-dementia/facts-figures
RISK FACTORS FOR COGNITIVE IMPAIRMENT/DEMENTIA

• Non modifiable: age; sex; genetics; family history
• 40% of dementia related to 12 modifiable risk factors
  – High blood pressure
  – Smoking
  – Diabetes
  – Obesity
  – Lack of physical activity
  – Poor diet
    - High alcohol consumption
    - Low levels of cognitive engagement
    - Depression
    - Traumatic brain injury
    - Hearing loss
    - Social isolation

EPIDEMIOLOGY OF COGNITIVE IMPAIRMENT/DEMENTIA IN INDIVIDUALS WITH DIABETES
ASSOCIATION BETWEEN DM AND CI/DEMENTIA

- Historical Cohort - Rochester, MN (1970-1984; N=1,455)
  - RR 1.66 for dementia; RR 2.27 for AD
- Canadian Study of Aging (1991-1992; N=5,574)
  - RR 2.03 for vascular dementia
- New York City Cohort (1999-2007; N=1,488)
  - HR 1.6 for AD; HR 5.4 for vascular dementia

Luchsinger, Ryan, Launer, 2016 – Diabetes in America; Chapter 24; Diabetes and Cognitive Impairment
ASSOCIATION BETWEEN DM AND CI/DEMENTIA

• Honolulu Asia Aging Study (1991-1994; N=2,574)
  – RR 1.5 for dementia; RR 1.8 for AD; RR 2.3 for vascular dementia

• Group Health Cooperative (1994-2004; N=2,067)
  – HR 1.40 for dementia

Luchsinger, Ryan, Launer, 2016 – Diabetes in America; Chapter 24; Diabetes and Cognitive Impairment
POTENTIAL MECHANISMS AND PATHWAYS LINKING DIABETES TO COGNITIVE IMPAIRMENT/DEMENTIA
POTENTIAL BIOLOGICAL MECHANISMS

• Cerebrovascular
  – Mini-strokes/White matter disease
  – Cerebral amyloid angiopathy
  – Inflammation
  – Demyelinating processes

• Non-Cerebrovascular
  – Hyperinsulinemia (insulin resistance)
  – Advanced glycation endproducts
  – Hypoglycemia

Luchsinger, Ryan, Launer, 2016 – Diabetes in America; Chapter 24; Diabetes and Cognitive Impairment
POTENTIAL SOCIO-BIOLOGICAL PATHWAYS

Pre-diabetes and Type 2 Diabetes

Health disparities
- Socioeconomic status
- Social network
- Built environment
- Food insecurity
- Ethnic/racial background
- Access to healthcare
- Control of multi-morbidity
- Medication adherence

Overweight & Obesity
- Metabolic alterations
- Vascular alterations

Aging

Multi-morbidity

Neuro-degeneration

Cognitive Impairments and Dementias

Gustafson, McFarlane 2018: Chapter 2; Type 2 Diabetes and Dementia
CLASSIFICATION OF COGNITIVE IMPAIRMENT/DEMENTIA IN INDIVIDUALS WITH DIABETES
THREE STAGE CLASSIFICATION – STAGE 1

• Mild changes in cognition
• May represent normal cognitive aging
• Unlikely to significantly interfere with ADLs
• May interfere with diabetes self management if regimen is complex
• Only detectable in neuropsychological testing

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016
THREE STAGE CLASSIFICATION – STAGE 2

• Mild to moderate cognitive impairment
• Testing shows cognitive impairment in one or more domains
• Does not meet criteria for dementia
• Subtle impairment in ADLs
• Can interfere with diabetes self management

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016
THREE STAGE CLASSIFICATION – STAGE 3

• Dementia
• Tends to occur in those 60 years or older
• Progresses over time
• Cognitive impairment in two or more domains
• Decline in executive function and impairment of ADLs
• Inability to understand or remember instructions
• Leads to poor diabetes self management

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016
SCREENING FOR COGNITIVE IMPAIRMENT/DEMENTIA IN INDIVIDUALS WITH DIABETES
AMERICAN DIABETES ASSOC. GUIDELINES

• Screen adults 65 years and older at initial visit, annually and as appropriate
  • MMSE
  • MiniCog
  • Montreal Cognitive Assessment (MOCA)
• Referral to behavioral health for formal cognitive/neuropsychological testing

ADA Guidelines; Diabetes Care Jan 2022
ESTABLISHING A DIAGNOSIS

• Detailed social history (assess effect of CI on function)
• Exclude other conditions (e.g., depression, hearing loss)
• Exclude organic causes
  • Hypothyroidism; Vit B12/Folate Def; Anemia; Hepatic dysfunction; Renal dysfunction; Hypercalcemia
• Consider age of the patient
  • <65 yrs, thorough eval for other underlying causes
• Brief cognitive assessment – MOCA, MMSE, MiniCog
• Refer and Follow up

Moulton, Diabetes & Primary care 2016
Question 2

• Which of the following are recommended tools for brief cognitive assessment in individuals with diabetes and cognitive impairment?

A- Montreal Cognitive Assessment (MOCA)
B- MiniCog
C- Mini Mental Status Exam (MMSE)
D- All of the above
Question 2 - Answer

• Which of the following are recommended tools for brief cognitive assessment in individuals with diabetes and cognitive impairment?

A - Montreal Cognitive Assessment (MOCA)
B - MiniCog
C - Mini Mental Status Exam (MMSE)
D - All of the above
PHARMACOLOGIC/NON-PHARMACOLOGIC INTERVENTIONS

• Few medications available for managing dementia in general
• None modify the underlying disease
• No treatments target CI in diabetes
• Blood pressure lowering and certain glucose lowering agents may be beneficial
  • Metformin; TZDs; DPP IV Inhibitors; GLP-1 agonists
• Diet/exercise may be beneficial
• Treatment of CVD risk factors may be beneficial

Calisaya & Moran, Type 2 Diabetes and Dementia; Chapter 12, 2018
PHARMACOLOGIC INTERVENTIONS FOR ALZHEIMERS

• Cholinesterase inhibitors
  • Mild to moderate AD
  • Donezepil; Galantamine; Rivastigmine

• Memantine
  • Moderate to advanced AD
  • Alone or in combination with cholinesterase inhibitors

• Aducanumab
  • FDA approved for mild AD

• Vitamin E (1000 IU BID may be beneficial)
Question 3

• Which of the following are true about treatment options for cognitive impairment in individuals with diabetes?

A- Few medications are available for managing CI
B- None modify the underlying disease process
C- Treatment of CVD risk factors may be beneficial
D- Diet and exercise may be beneficial
E- All of the above
Question 3 - Answer

• Which of the following are true about treatment options for cognitive impairment in individuals with diabetes?

A- Few medications are available for managing CI
B- None modify the underlying disease process
C- Treatment of CVD risk factors may be beneficial
D- Diet and exercise may be beneficial
E- All of the above
ASSISTIVE DEVICES FOR CI IN DM

1. Recording and alarming devices
   - Records reminder message
   - Photo albums with audio/video reminders
   - Automated pill dispensers
   - Vibrating or audio watch
   - Diabetes Sentry wrist alarm for tracking hypoglycemia

2. Insulin/Injectable devices
   - Insulin pens with memory of time/dose
   - Insulin pump

Hopkins, Shaver, Weinstock; Diabetes Spectrum 2016
ASSISTIVE DEVICES FOR CI IN DM

• 3. GPS tracking with emergency alarm

• 4. Talking glucose meters

• 5. CGM devices

• 6. Electrical use monitors
Case 1 - Revisted

• 72 year old woman with type 2 diabetes, hypertension, and hyperlipidemia
• Presents with poorly controlled diabetes and difficulty with self care
• Daughter states patient is having progressive difficulty remembering to take medications or test her sugars
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Conclusions

• Strong assoc. between diabetes and CI/dementia
• Potential pathways include cerebrovascular and non-cerebrovascular mechanisms
• Annual screening recommended for adults 65 years and older
• Brief screening tools include MOCA, MiniCog and MMSE
• No targeted treatment options are currently available
• CVD risk factor control and diet/exercise may be beneficial
• FDA approved medications for AD including cholinesterase inhibitors, memantine, and adacanumab may be options
Questions?