Drinking and Metabolic Disorders:
Type 2 Diabetes Mellitus and Metabolic Syndrome

BACKGROUND

The liver and the pancreas are responsible for producing the enzymes involved in breaking down the carbohydrates, fats, and proteins in food and turning them into energy. If these metabolites are not used immediately, the body stores them in the muscles, fat cells, or liver for later use.

Metabolic disorders is an umbrella term for conditions in which food metabolism is disrupted, either through problems in the liver or pancreas, or in the utilization of stored energy.

This *IARD Health Review* focuses on the two most common metabolic disorders, Type 2 diabetes mellitus and MetS.

The International Diabetes Federation estimates the prevalence of diabetes worldwide to be 8.3% [2], with Type 2 diabetes accounting for 90% of all cases [3].
- The global burden of disease attributable to diabetes in 2012 was 1.5 million deaths and 89 million disability adjusted life years (DALYs) [4].
- Individuals with Type 2 diabetes are at increased risk for kidney failure, stroke, cardiovascular disease, diabetic retinopathy, and amputation due to nerve damage and poor circulation to the feet [5].

MetS is estimated to affect at least 20% to 30% of the adult population in most countries [6]. Rates are higher in Latin America than in the U.S. and Canada or across Europe.
- The global burden of disease attributable to MetS is difficult to assess, as each of the defining components of MetS is a risk factor for cardiovascular disease, and individuals with MetS often develop diabetes [7].
- Individuals with MetS are at increased risk for atherosclerotic cardiovascular disease and Type 2 diabetes [8].

It is widely acknowledged that the increasing rate of obesity worldwide is driving an increasing rate in MetS, which in turn contributes to an increasing rate of Type 2 diabetes [9, 10] and cardiovascular disease [11].

Diabetes risk is also linked to genetic factors, age, ethnicity, and in some populations maternal malnutrition.

SUMMARY OF THE EVIDENCE

The relationship between alcohol intake and risk for Type 2 diabetes is characterized by a J-shaped or a U-shaped curve, similar to what is observed for cardiovascular disease and all-cause mortality.
- Moderate drinkers are at lower risk for Type 2 diabetes than abstainers and heavier drinkers [12-14].
- This relationship has been observed in both men and women [15, 16] and holds true across cultures and ethnic groups [17-19].
- Heavy drinking and heavy episodic drinking are associated with increased risk for Type 2 diabetes [20-25].

The relationship between MetS and alcohol consumption also follows a J-shaped curve.
- A protective effect has been described for moderate drinking and risk of MetS [22, 26-29], with some evidence suggesting that the benefit may be related to drinking in conjunction with meals [30, 31].
- Heavy drinking is associated with an increase in risk for MetS [19, 22, 32], as is heavy episodic drinking, particularly among occasional heavy drinkers [33].

MetS and Type 2 diabetes contribute to risk for other serious or life-threatening conditions and diseases.
- Individuals with Type 2 diabetes are at increased risk for kidney failure [4], stroke and cardiovascular disease (CVD) [34], diabetic retinopathy, and amputation.
- Individuals with MetS may have twice the risk for cardiovascular disease [11, 35] and five times the risk for Type 2 diabetes [36] compared with individuals without the syndrome.
- The cardioprotective benefits of moderate alcohol consumption may be especially important in metabolic disorder patients because of the prevalence of cardiovascular comorbidities within these populations [27].
- As alcohol intake increases, cardiovascular protection may be offset by increased risk for hypertension [37].

Mechanisms of action

The biological mechanisms underlying the relationship between moderate drinking and Type 2 diabetes and MetS have been well described.
- Alcohol consumption appears to improve insulin sensitivity without affecting insulin secretion [16, 38, 39], which helps to regulate plasma glucose levels [40]. High plasma glucose levels are a diagnostic marker for both Type 2 diabetes and MetS.
- Light-to-moderate alcohol consumption is associated with more favorable measures of fasting triglycerides, fasting glucose, and hemoglobin A1c among obese subjects [41] and among broader populations that include subjects with and without MetS [42].
- Moderate alcohol consumption is associated with an elevated blood concentration of high-density lipoprotein (HDL) [43-45]. Low HDL levels are associated with MetS and cardiovascular disease risk [27].

Among individuals with Type 2 diabetes or MetS, moderate consumption of alcohol may reduce the risk for other related diseases and improve disease outcomes.
- Moderate drinking appears to reduce the risk of cardiovascular disease [46] and cardiovascular deaths [14], and deaths from all causes among Type 2 diabetes patients [46].
- Elevated HDL cholesterol concentration, lower insulin levels and a lower risk of ischemic heart disease have been reported in association with moderate drinking among men, both with and without MetS [27].
- A decrease in the progression of atherosclerosis has been demonstrated in moderate drinkers with Type 2 diabetes [47].
- Heavy drinking, conversely, increases blood pressure [48] and triglycerides [49], both of which are among the features of MetS.

Daily moderate drinking as part of a high quality diet may improve Type 2 diabetes and MetS outcomes.
- A Mediterranean-type diet that includes daily moderate drinking has been associated with reduced cardiovascular mortality and all-cause mortality among patients with Type 2 diabetes. Furthermore, daily moderate drinking is reported to have the largest preventive impact on overall mortality among other identified components of the Mediterranean diet [50].
- Similarly, among patients with MetS, adherence to a Mediterranean-type diet that includes daily moderate drinking was associated with lower prevalence of MetS, progression of MetS, and several measures of individual MetS components, including abdominal adiposity, HDL cholesterol, triglycerides, fasting glucose, and insulin resistance [42].

There is evidence that harmful drinking patterns may interfere with treatment compliance among Type 2 diabetes patients [23] and worsen Type 2 diabetes outcomes [51].

Influences on the relationship between alcohol consumption and metabolic disorders

The relationship between drinking and metabolic disorders is moderated by age, gender, body mass index (BMI), diet quality, and physical activity.
- Age plays a role in risk of onset of Type 2 diabetes and MetS, as insulin resistance and glucose intolerance increase with age.
- However, the relationship between Type 2 diabetes and moderate drinking seems particularly robust in older adults [52].
- Some studies find that the protective effects of moderate alcohol consumption are greater for women than for men [24], with more significant reductions in risk for Type 2 diabetes.
- Obesity plays a substantial role in the development and progression of Type 2 diabetes [17, 53], and is a defining criterion for MetS.
- Physical activity significantly reduces the risk for obesity, MetS, and Type 2 diabetes. Among patients with MetS, moderate drinking combined with physical activity has a greater effect on MetS than moderate drinking alone [42].

METHODOLOGICAL CONSIDERATIONS

When interpreting research findings on risk factors and associated health outcomes, a number of methodological issues should be taken into consideration.

Confounding:

Confounding variables can obscure the true nature of the relationship between drinking and metabolic disorders, and need to be identified and controlled to the greatest extent possible.
- Age, gender, ethnicity, and weight/obesity status, as indicated by BMI, are differentially associated with both drinking and with metabolic disorders, or, more specifically, with conditions strongly related to a metabolic disorder, and may confound the relationship with drinking.

Underreporting:

Underreporting of consumption is a central concern of alcohol-related research. It is well established that survey respondents often underestimate their alcohol consumption. The magnitude of underreporting varies by respondent, context, and the approach used to measure consumption.

Misclassification of Drinkers:

Studies suggest that the underreporting of consumption can result in the misclassification of drinkers, especially between the low and moderate consumption categories. This misclassification can make it difficult to establish a clear relationship between low or moderate alcohol intake and disease outcomes. This, in turn, makes it difficult to identify definitive thresholds at which alcohol consumption increases the risk for specific diseases.

TERMS AND CONCEPTS

Insulin is a hormone, produced by the pancreas, which is released in response to an increase in blood glucose levels. Insulin controls the transport of glucose through the bloodstream into and out of the muscles, fat cells and other tissues in response to high or low glucose levels in the blood.

Diabetes mellitus refers to a class of diseases in which blood sugar levels are elevated over long periods of time, either through the failure of the pancreas to produce sufficient insulin or of cells to respond to insulin stimulation. There are three types of diabetes:

- Type 1 diabetes mellitus, formerly called insulin dependent diabetes, occurs when the pancreas loses its ability to produce sufficient insulin, and usually manifests itself in childhood or young adulthood.

- Type 2 diabetes mellitus, formerly called non-insulin dependent diabetes, occurs when tissue or red blood cells become resistant to insulin, often accompanied by reduced insulin secretion by the pancreas. Type 2 diabetes is also referred to as adult-onset diabetes, usually manifesting itself in adulthood.

- Gestational diabetes is a temporary condition of insulin resistance occurring during pregnancy to women with no previous history of diabetes. Women who have had Gestational diabetes have a higher risk of developing Type 2 diabetes later in life.

Metabolic syndrome (MetS) is a widespread disorder of the metabolic processes governing energy utilization and storage. Diagnosis requires three out of the following five correlated conditions: abdominal obesity, high blood pressure, high fasting plasma glucose levels, high serum triglycerides, and low levels of high-density (HDL) cholesterol.

Ranges for moderate and heavy drinking and metabolic disorders:

There is little consistency in the definitions used across research studies regarding "moderate" and "heavy" alcohol consumption. In some instances, definitions may include average volume, average frequency of alcohol consumption, or a combination of both. This lack of consensus on what constitutes moderate or heavy drinking can diminish cross-study comparability.

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Reviews

IARD Health & Policy Reviews cover the effects of alcohol consumption on health. They offer an overview of the relationship between drinking patterns and health outcomes, compile the key literature, and provide the reader with an extensive bibliography that refers to original research on each topic. The *Reviews* attempt to present the balance of the available evidence. They do not necessarily reflect the views of IARD or its sponsoring companies.

IARD is a not-for-profit organization dedicated to addressing the global public health issue of harmful drinking. Our mission is to contribute to the reduction of harmful drinking and promote responsible drinking worldwide. This is a problem that requires new insights, urgent action, and open dialogue. Central to IARD's work is our role as Secretariat of the Beer, Wine and Spirits Producers' Commitments to Reduce Harmful Drinking.

IARD

INTERNATIONAL ALLIANCE FOR
RESPONSIBLE DRINKING

action on alcohol and global health

The International Alliance for
Responsible Drinking (IARD)
The Jefferson Building
1225 19th Street NW, Suite 500
Washington, DC 20036

Phone: 1.202.986.1159
Fax: 1.202.986.2080
Email: info@iard.org
Web: www.iard.org