UNIVERSITI TEKNOLOGI MARA

THE RELATIONSHIP BETWEEN SERUM BISPHENOL A AND ATHEROSCLEROSIS BIOMARKERS IN PRIMARY CARE PATIENT WITH METABOLIC SYNDROME

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ABSTRACT

Bisphenol A (BPA) is an endocrine-disrupting chemical widely used in consumer products and has been linked to cardiovascular risk through oxidative stress and lipid metabolism disturbances. Individuals with metabolic syndrome (MetS), who already have underlying metabolic and cardiovascular dysfunction, may be especially vulnerable to these effects. This study aimed to evaluate serum BPA levels and their associations with oxidative stress biomarkers and atherogenic lipoproteins in patients with MetS. A cross-sectional study involving 193 MetS patients was conducted at an institutional primary care clinic in Selangor. Serum BPA levels were quantified via liquid chromatography–mass spectrometry (LC–MS). The concentrations of oxidative stress biomarkers (oxidized LDL [oxLDL] and isoprostane) and atherogenic lipoproteins (small dense LDL [sdLDL] and lipoprotein(a) [Lp(a)]) were assessed. Correlation analysis was used to examine the relationships between serum BPA and oxidative stress and atherogenic biomarkers. Simple and multiple linear regression analyses were conducted to determine the independent associations between serum BPA levels and each biomarker, adjusting for potential confounders such as age, sex, and metabolic parameters. Among the 193 samples, 79 (41%) had quantifiable BPA levels. The majority (92%) of these concentrations were below the tolerable daily intake (TDI) threshold of 0.5 ng/mL, whereas only 8% exceeded this limit, with concentrations ranging from 0.51 ng/mL to 1.36 ng/mL. No significant correlation was detected between serum BPA concentrations and log-transformed levels of sdLDL, Lp(a), isoprostane, or log-transformed oxLDL. Multiple linear regression analysis further confirmed the lack of association between BPA and these cardiovascular biomarkers. However, log-transformed total cholesterol, triglyceride, HDL, and LDL levels were independently associated with log-transformed sdLDL levels. In addition, log-transformed HDL was significantly positively associated with Lp(a) (β=63.26; 95% CI: 18.49 to 108.03; $p = 0.006$). Malay ethnicity was inversely associated with isoprostane levels (β=-64.32; 95% CI: -118.67 to -9.96; $p = 0.021$), whereas female sex was significantly associated with elevated log-transformed oxLDL levels (β=0.17; 95% CI: 0.01 to 0.33; $p = 0.040$). Serum BPA levels were low and not significantly associated with oxidative stress biomarkers or atherogenic lipoproteins in this MetS cohort. Significant associations were observed with conventional lipid measures, and selected demographic factors underscore the complex interplay of metabolic and genetic influences on cardiovascular risk. Longitudinal studies are warranted to further elucidate the role of BPA in cardiometabolic health.

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CHAPTER ONE
INTRODUCTION

1.1 Introduction

Bisphenol A (BPA) is a synthetic compound extensively utilized in the production of polycarbonate plastics and epoxy resins, materials commonly found in consumer products such as food containers, canned linings, toys, thermal receipts, and medical equipment (1). Human exposure to BPA occurs through ingestion, inhalation, or dermal absorption, with elevated risk among individuals involved in the manufacturing or handling of BPA-containing materials (2). BPA is classified as an endocrine-disrupting chemical (EDC) because of its ability to mimic or interfere with hormonal signalling, particularly estrogen pathways (3). Beyond endocrine disruption, BPA is increasingly recognized for its role in cardiovascular pathology, particularly atherosclerosis, where it contributes through oxidative stress, endothelial dysfunction, and inflammatory responses (4-6).

Atherosclerosis is characterized by lipid accumulation, chronic vascular inflammation, and oxidative damage (7). A pivotal event in this process is the oxidation of low-density lipoprotein (LDL) cholesterol into oxLDL, which promotes foam cell formation and plaque development (8). Small dense LDL (sdLDL) is particularly atherogenic because of its enhanced ability to penetrate the arterial intima and its greater susceptibility to oxidative modification (9, 10). Lipoprotein(a) contributes to atherogenesis by delivering cholesterol to vascular lesions and inhibiting fibrinolysis through its structural similarity to plasminogen (11, 12). BPA may further exacerbate these processes by impairing mitochondrial function and increasing reactive oxygen species, thus amplifying oxidative injury at the cellular level (13). However, limited research has examined how BPA exposure may influence these specific atherosclerosis-related biomarkers in human populations.

Metabolic syndrome (MetS) is a clinical condition comprising a cluster of interrelated cardiometabolic risk factors that significantly increase the risk of developing atherosclerotic cardiovascular disease. In Malaysia, MetS affects up to