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Urinary isoflavone and lignan phytoestrogen levels and risk of uterine fibroid in Jamaican women

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ABSTRACT

Background: Isoflavones and lignans are phytoestrogens, and therefore, are able to bind to and activate estrogen receptors. The resultant estrogenic or antiestrogenic effect is dependent on the concentration of these phytoestrogens relative to endogenous estrogens and the site of their action, among others. Thus, isoflavones and lignans act as selective estrogen receptor modulators; having a beneficial effect in some tissues while simultaneously causing deleterious changes in others.
Objective: This case-control study investigates the relationship between urinary concentrations of genistein, daidzein, equol, and enterolactone, and the presence of uterine leiomyomas (fibroids) in Jamaican women.
Design: Phytoestrogen concentration in spot urine samples from 157 uterine fibroid cases and 171 fibroid-free controls diagnosed by ultrasonography, were assessed by Time-resolved Fluoroimmnoassay. Statistical evaluations were performed using SPSS 12.0.
Results: The median concentration of urinary enterolactone was significantly different between uterine fibroid cases and controls ($p = 0.029$). However, this was not observed to affect risk of uterine fibroid, as trends across quartiles of urine enterolactone did not differ significantly between cases and controls. Median urinary genistein ($p = 0.510$), daidzein ($p = 0.838$), equol ($p = 0.621$), total isoflavones (0.510) and total phytoestrogens ($p = 0.084$) were similar for both groups. Binary logistic regression analysis of quartiles of urine genistein, daidzein, equol, enterolactone, total isoflavones, and total phytoestrogens showed no association with uterine fibroid.
Conclusions: Uterine fibroid cases had a higher median urine concentration of enterolactone compared with controls. However, this was not observed to affect ones risk of fibroid. Neither was urine genistein, daidzein, equol total isoflavones, and total phytoestrogens observed to be associated with risk of uterine fibroid.

1. Introduction

Isoflavones and lignans are phytoestrogens renowned for their ability to simulate the action of steroid hormones, via estrogen receptor activation [1]. Isoflavones, unlike the more ubiquitous lignans, tend to be restricted to leguminous plants, of which soybean is the highest known source [2]. Asian populations that traditionally consume soy products excrete high urinary levels of phytoestrogens [3]. In contrast, populations that consume soy products less regularly, e.g., Americans and Europeans, excrete significantly lower levels of these metabolites [4,5]. The increased substitution of animal-based constituents in foods with suitable plant-based derivatives could change the overall exposure of some populations to phytoestrogens. Therefore, individuals who adopt a more macrobiotic diet or simply consume more plant-based food derivatives should have a higher level of phytoestrogen exposure.

The diet of Jamaicans have become one high in processed or fast foods and low in fiber and complex carbohydrates from freshly

Abbreviations: GnRH, gonadotropin-releasing hormone; TR-FIA, time-resolved fluoroimmunoassay; BMI, body mass index; CI, confidence interval; OR, odds ratio.

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harvested vegetables, fruits, and starchy foods [6,7]. However, the traditional diet of complex carbohydrates and fiber from yams, potatoes, green plantain, and bananas is still adhered to by some individuals [8,9]. Consequently, Jamaicans on a traditional diet may, therefore, differ from other western populations in their exposure to phytoestrogens, due to the bioavailability of these phytochemicals when consumed. Jackson et al. investigating phytoestrogen exposure and risk of prostate cancer in Jamaican men found that excretion of daidzein, equol, and enterolactone was generally higher when compared to some other western multiethnic populations with low intakes of soy products [10]. Importantly, they observed a strong correlation between equol production and sugary foods. This is supported by other studies which suggest that increased carbohydrate consumption increases enteric fermentation and bioconversion of daidzein to equol [10,11,12].

Studies of the effect of phytoestrogens on the hormone-dependent conditions such as menopausal symptoms, cancer and cardiovascular disease are widespread [2]. However, fewer investigations have looked into their consumption and risk of fibroid. Uterine fibroids (leiomyomas) are responsible for severe morbidity in many populations, causing symptoms such as heavy and irregular menstrual periods, infertility, and spontaneous abortions, frequent urination, kidney obstructions and other problems associated with the size and location of the fibroid [13]. Even with non-invasive treatment options, such as with gonadotropin-releasing hormone (GnRH) agonists, fibroids are the sole leading cause for hysterectomies in many countries [14,15]. Two studies, one involving women in the United States and the other in Japan, found no association between fibroid risk and urinary isoflavone excretion [16,17]. However, both studies were limited in that the former reported low intakes of soy isoflavones while the latter did not have significant power to detect a small association. A slight inverse relationship was noted with lignan excretion in the study involving American women [16]. This case-control study examined reported dietary data and the urinary levels of genistein, daidzein, equol, total isoflavones, enterolactone, and total phytoestrogens of 'healthy' Jamaican women and fibroid incident cases and thereby evaluated reduced or increased risk of the disease in this population.

2. Subjects and methods

2.1. Study population

Participant recruitment for this study was conducted in the vicinity of Kingston and St. Andrew (Fig. 1). The case-control study was described to participants who were asked to sign a consent form at the time of screening stating their agreement to participate in the study. Women were screened at the Diagnostic Unit of the University Hospital of the West Indies, where their uterine fibroid status was diagnosed by abdominal and/or vaginal ultrasonography. Participants were also required to donate fasted spot urine and blood samples but for the nested case-control study only specimens collected from participants that fulfilled the study criteria were analyzed. Persons were eligible if they were not pregnant, had not used antibiotics or changed their diet within the previous six months, and were not on a special diet. It was estimated that to detect 20% change in risk (that is, an odds ratio of 0.80 or 1.20) with 80% power and at 5% significant level, a sample of 170 was required in each group. A total of 375 women (20–75 years) were screened, of which 174 were confirmed to be cases and 201 healthy controls. Of these, 157 (90.2%) cases and 171 (85.1%) controls were eligible to participate.

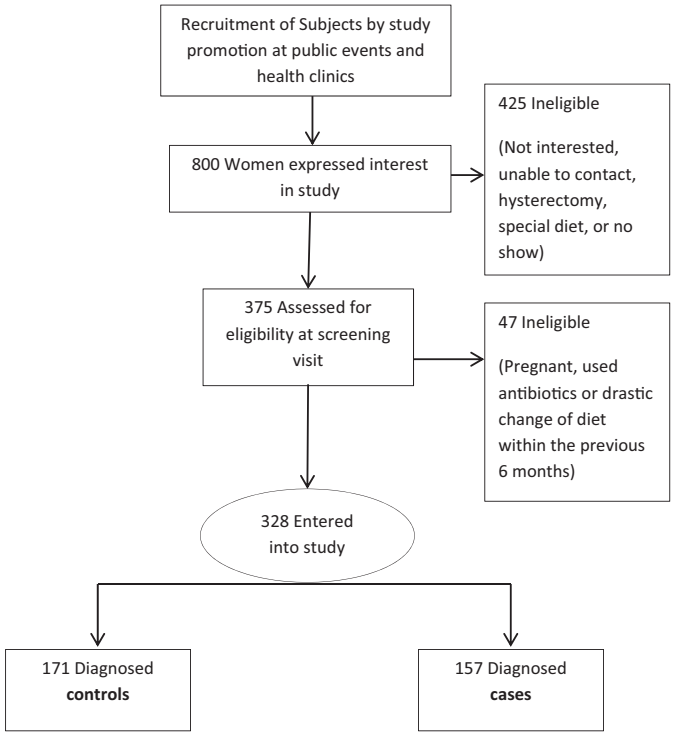

Fig. 1. Flowchart of recruitment process.

2.2. Phytoestrogen analysis

The analysis of urinary genistein, daidzein, equol, and enterolactone on spot urine samples, obtained after an overnight fast, was performed by time-resolved fluoroimmunoassay (TR-FIA) using a Victor1420 multilabel counter (PerkinElmer Inc.). Urinary levels of the metabolites are reported here as nanomoles per milligram (nmol/mg) of creatinine excreted. The method employed has been previously described in detail [10]. The intra- and inter- assay coefficients of variation for the phytoestrogen metabolites ranged from 4.4 to 11.8 and 5.8 to 14%, respectively.

2.3. Participant interviews and dietary data

Participants were subjected to in-person interviews to obtain detailed information on socio-demographic factors, menstrual, and reproductive history, family history of fibroids, cigarette, and alcohol use, oral contraceptive use and dietary intake of selected foods and supplements over the past 6 months. Anthropometric measures of weight and height were recorded as follows: Weight was recorded to the nearest 0.1 kg using a Delta meter Mechanical Balance scale after each participant removed shoes. Height was measured without shoes on a floor stadiometer fitted with a spirit level, to the nearest 0.1 cm. Waist and hip circumferences were measured to the nearest cm using a tape measure according to standard techniques. Body mass index (BMI) was computed as weight (in kilograms) divided by height (in meters, squared).

2.4. Statistical analysis

Chi-square statistics (for categorical variables) and independent-sample *t*-test (for continuous, normally distributed data) were used to examine demographic, medical history, and social factor differences between uterine fibroid cases and non-fibroid controls. Data on the frequency of consuming foods were correlated to the urine excretion of genistein, daidzein, equol,

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