



## Hot flushes and reproductive hormone levels during the menopausal transition



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### ABSTRACT

**Introduction:** Evidence suggests that hot flushes are associated with fluctuating levels of oestradiol (E2) during menopause, as well as changes in the levels of follicle-stimulating hormone (FSH) and inhibin B. The relationship between hot flushes and anti-Müllerian hormone (AMH) is unknown.

**Aim:** To examine specific hormone levels and ethnic differences in relation to hot flushes.

**Methods:** Data were drawn from 108 women aged 40–59 years. There were three groups of participants: European women in London, UK; Bangladeshi women in Sylhet, Bangladesh; and Bangladeshi women who had migrated to London as adults. Symptom information was collected via questionnaires. Serum blood samples were collected to detect inhibin B, AMH, FSH, and E2.

**Results:** AMH and FSH were significantly associated with the experience of hot flushes in the past 2 weeks. Inhibin B and E2 were not associated with hot flushes. Body mass index (BMI), ethnicity, and education level were associated with both the occurrence and the frequency hot flushes. Menopausal status was also associated with the frequency of hot flushes.

**Conclusion:** Relationships between AMH, FSH and symptoms are indicative of women's progress through the menopausal transition. The influence of BMI and education suggest that lifestyle changes may contribute to the management of symptoms. This merits further research.

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### 1. Introduction

The menopausal transition is marked by significant changes in reproductive hormone levels with an eventual decline in levels of reproductive steroids and an increase in gonadotrophins [1–4]. Hormonal changes can be observed as early as the third decade of life for most women, emphasizing the processual nature of reproductive ageing [5–7]. Menopause is accompanied by a suite of symptoms that vary in occurrence and severity among and between women, with hot flushes being among the most troublesome [4,8]; up to 80% of women experience hot flushes in the U.S. and Britain [9,10]. Hot flushes are associated with declining levels of oestrogen

[11], purportedly because a decline in this hormone is associated with a narrowing of the thermoneutral zone between the core body temperatures that trigger shivering and sweating [12]. When the sweating threshold is lowered by hormonal changes, women sweat more easily in response to increases in core body temperature [13].

Understanding the relationship between hot flushes and hormonal changes is complicated by a lack of consistency in the results found in several studies. Most theories have concentrated on oestrogen rather than any other hormone because of its known role in thermoregulation [11,13]. Even here, however, the picture is far from clear. For example, oestrogen levels do not necessarily differ significantly between asymptomatic and symptomatic women and are not predictive of symptoms during the climacteric [14,15]. Hot flushes are also closely timed with luteinising hormone (LH) pulses, which might suggest that they are related in some way to gonadotrophin-releasing hormone (GnRH) synthesis. Rance et al. [16] suggest that hot flushes are caused by the

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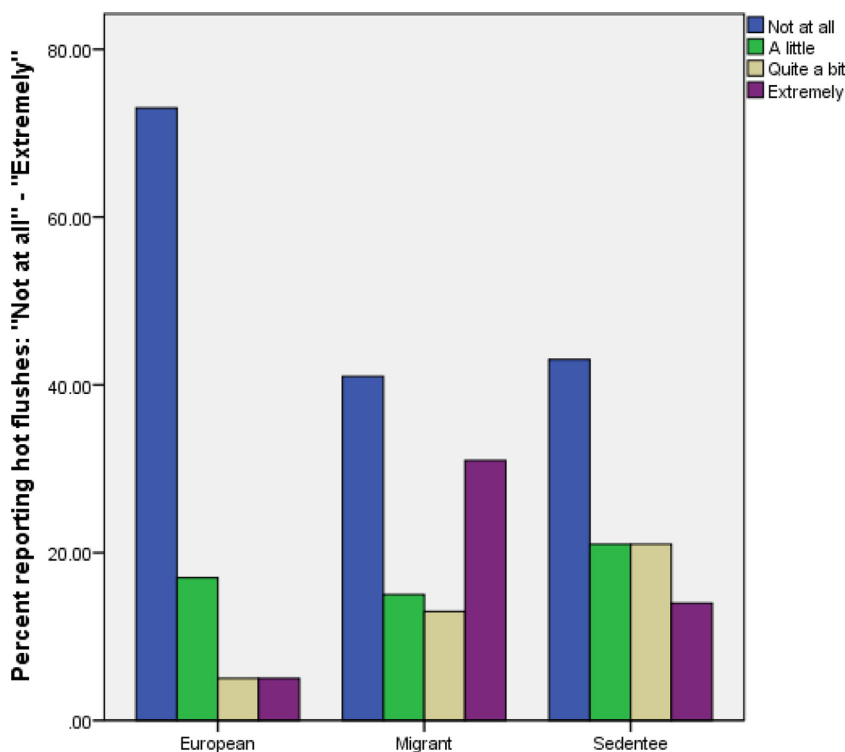


Fig. 1. Percentage of women reporting hot flushes as “not at all,” “a little,” “quite a bit,” or “extremely” during the past two weeks by group.

activation of kisspeptin/neurokinin B/dynorphin (KNDy) neurons following post-menopausal oestrogen withdrawal because these neurons modulate GnRH synthesis, express oestrogen receptors, and are hypertrophied in post-menopausal women. Such theories need further testing.

Many studies have demonstrated variation in age at menopause as well as differences in the experience of menopausal symptoms among women of different ethnicities [8,17,18]. Median ages at menopause range from 47 to 53 years among different populations, most likely due to significant environmental variation between populations in, for example, nutritional intake and exposure to diseases during childhood, energy expenditure, parity, and smoking rates [19]. There also appear to be differences in menopausal age because of allelic variations [20–22]. We have previously reported that women of Bangladeshi origin – those still living in Bangladesh and migrant women who moved to London during adulthood – had significantly earlier ages at menopause compared to London women of European origin [23]. These data are confirmed by Begum et al. [24], who found that age-matched Bangladeshi non-migrants and adult migrants had levels of inhibin B, AMH, FSH, and  $E_2$  that demonstrated an earlier age-related decline in ovarian reserve when compared to women of European origin.

There is a large range of individual and population variation in women's experience of hot flushes [25–27]. Differences in the prevalence of hot flushes have been reported by ethnicity, with African-American and Hispanic women reporting the highest frequency, and southeast Asian women reporting the lowest [9,28–30]. In our own studies of vasomotor symptoms among Bangladeshi and European women, we have found differences in the experience of hot flushes between middle class Hindu and Muslim women living in Bangladesh that appear to be related to differences in clothing and patterns of prayer. Islamic forms of prayer involve the physical exertion of repeated bending and kneeling [31]. So far, however, we have not yet explored relationships between levels of reproductive hormones and the experience of hot flushes among the same groups of women we have previously

studied. This paper therefore investigates the association between inhibin B, AMH, FSH, and  $E_2$ , and the occurrence and frequency of hot flushes among two groups of Bangladeshi women living in Bangladesh and the UK, and a comparative group of women of European origin living in London. To our knowledge, no prior papers have explored the relation between AMH and hot flushes. We hypothesized an increased probability of hot flashes and increasing hot flash frequency in association with lower levels of inhibin B, AMH, and  $E_2$ , and higher levels of FSH while controlling for other variables known to be associated with hot flushes. We also hypothesized a higher likelihood of hot flashes in the Bangladeshi populations.

## 2. Methods

### 2.1. Study participants

Participants ( $n=108$ ) who volunteered to give blood were drawn from a larger sample of women ( $n=485$ ) recruited into a study of the menopausal transition in Bangladesh and London [23,31,32]. These included: Bangladeshi women living in Sylhet, northeast Bangladesh (‘sedentees’), Bangladeshi women living in London (mostly in Camden and East London) who migrated to London as adults (adult migrants), and women of European origin living in London (Europeans). The subsample analysed here comprises sedentees ( $n=36$ ), adult migrants ( $n=53$ ), and Europeans ( $n=50$ ). In Sylhet, women were recruited through personal contacts and word of mouth while, in London, Bangladeshi migrants were recruited through community centres and word of mouth. The European women in London lived in similar neighbourhoods as the migrants, and were recruited through advertisements in local newspapers and flyers advertising the study. Eligibility criteria included: ages 40–59, no exogenous hormone use (hormone therapy or contraceptives) in the last 3 months, not currently lactating or pregnant, and no previous medical history of oophorectomy,

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