Systemic inflammation and suicide risk: cohort study of 419 527 Korean men and women

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ABSTRACT

Background  Data from only one study have been used to examine the relationship between systemic inflammation and later suicide risk, and a strong positive association was apparent. More research is needed, particularly looking at gender, not least because women are seemingly more vulnerable to inflammation-induced mood changes than men.

Methods  The Korean Cancer Prevention Study had a cohort of over 1 million individuals aged 30–95 years at baseline examination between 1992 and 1995, when white blood cell count, our marker of systemic inflammation, was assessed.

Results  A mean of 16.6 years of mortality surveillance gave rise to 1010 deaths from suicide in 106 643 men, and 1019 deaths from suicide in 312 884 women. There was little evidence of an association between our inflammation marker and suicide mortality in men after multiple adjustments. In women, however, those in the second inflammation quartile and higher experienced around 30% increase risk of death (HR 1.35; 95% CI: 1.11–1.64).

Conclusions  Higher levels of systemic inflammation were moderately related to an elevated risk of suicide death in women but not in men.

INTRODUCTION

The global burden of suicidal ideation, hospitalisation, and completion is considerable.1 While the psychosocial origins of suicide are becoming increasing well understood,2–3 with the exception of selected characteristics,4 7 comparatively little is known about its biological origins. Findings from studies using different designs have implicated systemic inflammation in the occurrence of suicide. Thus, in cohort studies, elevated levels of baseline inflammatory markers have been linked to depression and psychological distress8 which themselves are well-established risk factors for suicide.5 9 Additionally, pathological studies reveal that victims of suicide have higher cytokine levels relative to non-suicide controls.10

There is also some evidence of gender differences in these observations. Thus, although it is not a universal observation,11 there is a suggestion that women tend to be more vulnerable to inflammation-induced mood changes, with transient elevations seemingly eliciting a more pronounced sense of loneliness and social disconnection.12 We therefore hypothesised that inflammation may be more strongly associated with suicide risk in women than in men.

We recently reported a three-fold elevated risk of suicide death in people in the highest inflammation group;13 however, owing to a low number of events we were not able to examine gender-specific effects and the generalisability of this finding from a European population to non-Western countries is uncertain. Our objective in the present study, therefore, was to examine the association of inflammation with suicide mortality in a cohort study of over 400 000 Korean men and women. With South Korean women having the highest suicide death rate worldwide and men being ranked third, the country provides an ideal setting in which to enhance understanding of suicide aetiology.14 14

METHODS

Described in detail elsewhere,15 the Korean Cancer Prevention Study is a prospective cohort study established to identify environmental risk factors for major causes of death in more than 1 million people. In brief, the cohort comprises government employees and their dependents who were registered with the Korea National Health Insurance Service.

At study baseline (1992–1995), blood samples were obtained after an overnight fast with white blood cell counts, our marker of inflammation, quantified by automated blood cell counters (Beckman Coulter, Fullerton, California) in hospital laboratories. Cell counts are expressed in Système International d’Unités (×109 cells/L). Each hospital followed the quality control procedures of the Korean Association of Laboratory Quality Control.

Covariate data were assessed using standard protocols. Weight and height of each study member were measured directly in light clothing with shoes removed, and body mass index calculated in the usual manner (weight in kilograms divided by height in metres squared). Based on existing definitions,16 diabetes mellitus was denoted by a blood glucose of ≥126 mg/dL and/or self-report of either physician diagnosis or medication usage, and hypertension by a systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg, or the use of blood pressure lowering medication. With the study member present, completed questionnaires were scrutinised by research workers and, where necessary, clarification sought. Smoking (current smokers, former and never) and exercise (yes, no) were self-reported as was current total daily alcohol consumption, expressed as number of glasses per week of ‘Soju’. Comparable to vodka, soju is the most popular alcoholic beverage in Korea (one glass contains about 12 g of ethanol). Alcohol consumption was categorised: non-drinker (0 g/day), light
drinking (124.9), moderate drinking (25–49.9), heavy drinking (50–99) and very heavy drinking (>99). Our measure of socioeconomic status was the monetary contribution per year, in South Korean “Won” (W1112=US$1.00), made by the employee to their medical insurance scheme. This is means derived, being based on employee’s income plus assets, such as ownership of property and an automobile; a higher contribution therefore denotes higher socioeconomic status.

A computerised search of death certificate data from the National Statistical Office in Korea was performed and trained recorders extracted cause according to the International Classification of Diseases, Tenth Revision (suicide codes: E95, and X60–X84). Of a total of 1 329 525 study members, 878 367 had data on white cell count. Exclusions of people with implausible values and those with a baseline diagnosis of cancer or cardiovascular disease resulted in an analytical sample of 419 527. We summarised the relation between white cell count and suicide mortality using Cox proportional hazards regression. To examine if gender was an effect modifier in the inflammation–suicide relation, we created an interaction term and compared this more complex model with that described, and other mental health problems, as well as being implicated in the occurrence of suicide, it is a possible mediating factor in the inflammation–suicide relation. Unfortunately, we did not have sufficiently good indicators of mental health in the present study to explore this issue. Second, white blood cell count is likely to be elevated in the presence of an infection like the common cold on which we did not collect data. If the positive relation between white blood cell count and suicide in women was generated by acute infection one would anticipate an elevated risk in the highest blood cell count group only; however, raised suicide rates are in fact apparent across quartiles 2–4, so confounding by infection seems very unlikely.

Using the present data set, we have previously confirmed known relationships such as an association of smoking, high alcohol consumption and poverty with suicide mortality. While these results increase our confidence in the present novel findings for inflammation and suicide, our hypothesis requires further testing. With suicide mortality being rare, the utilisation of the more common suicide attempt via, for instance, hospital admission, would therefore have utility in this context, as would the use of other markers of systemic inflammation such as C-reactive protein and interleukin 6.
Correction notice This article has been corrected since it first published online. The open access licence type has been changed.

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Competing interests None declared.

Patient consent Detail has been removed from this case description/ these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

Ethics approval The Institutional Review Boards of Yonsei University and the Johns Hopkins University Bloomberg School of Public Health approved the study.

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REFERENCES