Scandinavian Journal of Pain 15 (2017) 1–7

Contents lists available at ScienceDirect

Scandinavian Journal of Pain

journal homepage: www.ScandinavianJournalPain.com

Observational study

Diabetes mellitus and hyperlipidaemia as risk factors for frequent pain in the back, neck and/or shoulders/arms among adults in Stockholm 2006 to 2010 – Results from the Stockholm Public Health Cohort

Oscar Javier Pico-Espinosa[a], Eva Skillgate[b,c], Giorgio Tettamanti[a], Anton Lager[d], Lena W. Holm[a,e,*]

[a] Unit of Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
[b] Unit of Cardiovascular Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
[c] Naprapathögskolan – Scandinavian College of Naprapathic Manual Medicine, Stockholm, Sweden
[d] Department of Public Health Sciences, Karolinska Institutet, Centre for Epidemiology and Community Medicine, Stockholm, Sweden
[e] Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

HIGHLIGHTS

- Hyperlipidaemia may be associated with the risk of back, neck and/or shoulder pain.
- Diabetes may be a risk factor for back, neck and/or shoulder pain among men.
- Metabolic conditions may be associated with the risk of musculoskeletal pain.

ARTICLE INFO

Article history:
Received 26 August 2016
Received in revised form 28 October 2016
Accepted 13 November 2016

Keywords:
Diabetes mellitus
Hyperlipidaemia
Back pain
Neck pain
Shoulder pain

ABSTRACT

Background and aims: Frequent back, neck and/or shoulder pain (BNSP) are common conditions which pose high burden for the society. Results from previous studies suggest that diabetes and hyperlipidaemia may be associated with a higher risk of getting such conditions, but there is in general, few studies based on longitudinal designs. The aim of this study was therefore to compare the risk of developing frequent BNSP in men and women with and without diabetes and/or hyperlipidaemia.
Methods: A longitudinal study based on the Stockholm Public Health Cohort was conducted based on subjects aged 45–84, who were free from pain at the mentioned sites in 2006 and followed up until 2010. The data in the current study is based on questionnaires, except socioeconomic status which was derived from Statistics Sweden. The exposure diabetes and hyperlipidaemia was self-reported and, a categorical variable was created; without any of the conditions, with hyperlipidaemia only, with diabetes only and with both conditions. The outcome frequent BNSP was defined using the following questions in the questionnaire in 2010: *"During the past 6 months, have you had pain in the neck or upper part of the back?"*, *"During the past 6 months, have you had pain in the lower back?"*, and *"During the past 6 months, have you had pain in the shoulders/arms?"*. All questions had three possible response options: no; yes, a couple of days per month or less often and; yes, a couple of days per week or more often. Those who reported weekly pain to at least one of these questions were considered to having frequent BNSP. Binomial regressions were run to calculate the crude and adjusted risk ratio (RR) in men and women separately. Additional analysis was performed in order to control for potential bias derived from individuals lost to follow-up.
Results: A total of 10,044 subjects fulfilled the criteria to be included in the study. The mean age of the sample was 60 years and evenly distributed by sex. After adjusting for age, body mass index, physical activity, high blood pressure and socioeconomic status, the RR for frequent BNSP among men with diabetes was 1.64 (95% CI: 1.23–2.18) and 1.19 (95% CI: 0.98–1.44) for hyperlipidaemia compared to men with neither diabetes nor hyperlipidaemia. Among women the corresponding RRs were 0.92 (95% CI: 0.60–1.14) and 1.23 (95% CI: 1.03–1.46). Having both diabetes and hyperlipidaemia at baseline was not associated with increased risk of frequent BNSP. Diabetes and hyperlipidaemia seems to be associated

* Corresponding author at: Unit of Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Nobels väg 13, Box 210, SE-171 77 Stockholm, Sweden. Tel.: +46 8 524 870 23; mobile +46 704 82 74 79.
E-mail address: lena.holm@ki.se (L.W. Holm).

http://dx.doi.org/10.1016/j.sjpain.2016.11.005

with an increased risk for frequent BNSP and the risk may differ between men and women. Behaviours and/or biological underlying mechanisms may explain the results.
Conclusions: This study suggests that metabolic diseases such as diabetes and hyperlipidaemia may have an impact on the pathophysiology of frequent BNSP and thus, contributes to the knowledge in musculoskeletal health. Furthermore, it confirms that men and women may differ in terms of risk factors for BNSP.
Implications: Health professionals should contemplate the results from this study when planning primary prevention strategies.

1. Introduction

Pain in the back and the neck represents a high burden for the healthcare systems, the society and individuals with the conditions, especially in developed countries, where its occurrence has increased in the past years positioning it now as one of the top contributors of disability adjusted life years [1]. Data from various studies have reported prevalence of between 4.4% and 13% for neck pain [2–4] and between 10.8% and 21.1% for back pain in the past 3 months [5]. The back and neck region involve multiple structures, all of them being potentially prone to suffer from injuries and/or pain of diverse origin [6,7] and when it comes to neck pain, the shoulder region is often involved.

Various authors have investigated the aetiology of pain in these three sites, having in common that none of them have found strong associations, making frequent back, neck and shoulder pain (BNSP) a relatively unexplored area of knowledge in which biological and environmental factors are to be considered. Among the reported risk factors for these conditions are female sex [8], older age [4], smoking [9], high job strain and job characteristics [10], high body weight [11], previous episodes of pain [10], psychological stress [12,13] and depression [14]. In addition, previous studies based on the Stockholm Public Health Cohort (SPHC) indicate that physical inactivity [15,16] and income [17] may be associated as well. Given that nowadays it is well accepted that multidisciplinarity is fundamental when it comes to the prevention and treatment of these conditions [18], a widened knowledge of risk factors may support new approaches.

Furthermore, results from previous cross-sectional studies indicate higher occurrence of pain of musculoskeletal origin among individuals with cardiovascular conditions such as atherosclerosis, high blood lipids, diabetes and glucose intolerance [5,19–21] but these associations have been scarcely explored in longitudinal studies [22,23]. Different explanations have been proposed as the link between cardiovascular conditions and pain, among them, the occlusion of lumbar or sacral arteries for the case of high blood lipids [18], deleterious effects of advanced glycation end products in the intervertebral discs [24,25], and inflammatory and immune responses originated by either mechanical or chemical insults [26]. Similarly, diabetes and hyperlipidaemia have been linked with inflammatory biomarkers such as TNF-α [27,28]: it is likely that the tissues of the musculoskeletal system can be target of such inflammation processes derived from the mentioned diseases.

The aim of this study was to compare the risk of developing frequent BNSP in men and women with and without diabetes and/or hyperlipidaemia; and based on that, contribute to the knowledge regarding the aetiology of musculoskeletal pain.

2. Material and methods

2.1. Study population

This cohort study is based on data from the Stockholm Public Health Cohort (SPHC), in which a postal and web based questionnaire that collects information from a random sample of the general population between 18 and 84 years in Stockholm was used. In 2006, 19,301 individuals aged between 45 and 84 participated in the study; 4 years later a follow-up survey was sent, which was answered by 15,290 (response rate 79%). The survey was available in six languages apart from Swedish in order to capture the actual distribution of the population in Stockholm [29].

For the present analysis, subjects who had responded both in 2006 and 2010, being above 45 and up to 84 year and who were free from frequent BNSP pain were included. Participants were then classified as exposed or unexposed based on self-reported information on high blood lipids and diabetes mellitus. The abovementioned age limit was set because the prevalence of diabetes and hyperlipidaemia is known to be uncommon among younger people. The selection of the study population, was further based on two questions in the 2006 questionnaire: "*During the past 6 months, have you had pain in the neck, shoulders or arms?*" with five possible answers: no; yes, a couple of days in the past half year; yes, a couple of days per month; yes, a couple of days per week or; yes, every day. The same formulation was used to ask about low back pain. These two variables were combined so that those individuals who answered any of the three first options of answers to both questions formed the study population that was followed for 4 years, and thus constitute the study base ($n = 10{,}044$).

2.2. Exposure and outcome definitions

Individuals with diabetes or hyperlipidaemia were identified using the question: *"have you received any of the following diagnosis by a doctor?"* Additionally, the person's age at diagnosis was asked. Both exposures were combined to create four categories: those without any of the conditions, those with only hyperlipidaemia, those with only diabetes and those with both diabetes and hyperlipidaemia. In 2010, the outcome frequent BNSP was defined using the following three questions: *"During the past 6 months, have you had pain in the neck or upper part of the back?"*, "*During the past 6 months, have you had pain in the lower back?*", and *"During the past 6 months, have you had pain in the shoulders/arms?"*. All questions had three possible response options: no; yes, a couple of days per month or less often and; yes, a couple of days per week or more often. Those who reported weekly pain to at least one of these three questions were considered as having frequent BNSP.

2.3. Confounders

The following potential confounders were selected from the questionnaire in 2006 based on its relevance: age, socioeconomic status, body mass index (BMI), physical activity level, smoking habits, receiving treatment for high blood pressure, alcohol intake and psychosocial stress. Socioeconomic status was categorized according to the information from Statistics Sweden based on occupation and education [30]. Physical activity level was self-reported and dichotomized as regular and not regular referring to the past 12 months. Smoking habits was categorized as

currently daily smoker, previously regular smoker (daily for at least 6 months) and, never daily smoker.

Receiving treatment for high blood pressure was defined using the question: *"Are you currently being treated for high blood pressure?* Where the option "No" was considered as no high blood pressure, and the options yes, but only with recommendations on change in lifestyle habits and yes, medications for high blood pressure, considered as yes. Risky alcohol intake was dichotomized using the cut off points 168 g/week (14 standard drinks) or more and 108 g/week (9 standard drinks) or more for men and women respectively; this quantity was estimated using information regarding type, amount and frequency of alcohol intake in a regular week. The cut-off points were based on a previous report from the Public Health Agency of Sweden [31]. Psychological stress was calculated and dichotomized based on the 12 questions from the General Health Questionnaire, using the scoring system 0-0-1-1, with 3 or more points indicating the presence of it [32]. Age and body mass index were used as continuous variables, the latter calculated based on self-reported weight and height and categorized; only 0.9% of the sample had a body mass index less than 18.5 and therefore that category was merged with the one of normal range for the presentation of the baseline characteristics of the study population.

2.4. Statistical analysis

Log-binomial regression models were run for these analyses using the software SPSS version 22, separately for men and for women, and the results are expressed in terms of risk ratio (RR) with 95% confidence interval (CI). First, the crude association between the exposures and the outcome was estimated. Following Rothman's method [33], the beta coefficient was annotated and then the potential confounders were introduced in the model, one at a time: in case of a change of 10% of more of the original beta coefficient, that variable was considered a confounder and later on included in the final multivariable model. Age, body mass index, physical inactivity, high blood pressure and socioeconomic status were significant confounders.

Since the outcome was constructed based on three pain sites, an individual analysis for each site could have provided hints on whether the observed results were restricted to one or two specific locations. However, it was observed that pain in these locations overlap to a great extent: among the persons with neck pain 62.1% also reported shoulder pain and 51.2% also reported back pain; among those with shoulder pain, 56.3% and 42.5% also reported neck and back pain respectively and; among those with back pain, 44.2% had shoulder pain and 48.3% had neck pain. Therefore, in the main analyses the outcome was defined as frequent pain at any site.

The occurrence of the outcome was stratified by duration of the exposures (5 years or earlier and 6 years or later, since the diagnosis). Chi-squared test was used to assess whether there was a difference in the occurrence of pain in terms of the duration of the exposures respectively (p-value of 0.768 for diabetes and 0.528 for hyperlipidaemia). Although there was a slightly higher occurrence of frequent BNSP among those who had been diagnosed with the exposure more than 6 years ago (both for diabetes and hyperlipidaemia), these differences were not statistically significant and this variable was not considered in the main analysis.

The analyses were repeated using a more stringent definition of "free from disease" in which those with monthly BNSP were excluded ($n = 2261$), based on the hypothesis that those individuals were in the pathway to become cases and therefore would dilute the associations. Additionally, based on the information from lost to follow-up, two possible scenarios were simulated: in the first one, it was assumed that all those individuals who did not respond in 2010 developed frequent BNSP and; in the second one, it is assumed the contrary situation: that none of them developed the outcome.

3. Results

3.1. Characteristics of the study population

A total of 10,044 persons were free from frequent pain in the back, neck and/or shoulder/arms in 2006 (5021 men and 5023 women). The characteristics of the study population are presented in Table 1. Here is presented the information based on the number of observations without missing data in the variables included in the adjusted model ($n = 8666$). The population was evenly distributed in terms of sex, the mean age was 60.0 years for men (SD: 9.4) and 59.5 years for women (SD: 9.5), for both men and women the majority belonged to the categories 50–59 and 60–69 years old. The average body mass index was 26.1 (SD: 3.5) for men and 24.7 (SD: 4.0) for women (data not shown). Almost half of the men were overweighed, whereas the majority of women had a low/normal BMI. Almost half of them had never been regular smoker (daily smoker for at least 6 months), three out of ten reported having risky alcohol intake, almost one quarter were receiving some form of therapy for high blood pressure, more than forty percent exercised regularly (44.2%), around one out of ten reported psychological stress and the prevalence of diabetes and hyperlipidaemia were 5.2% and 15.5% respectively.

Among men, the majority were professionals and intermediate non-manual employees. Among women, intermediate non-manual employees was the most common socio-economic category followed by assistant non-manual employees.

3.2. Main results

3.2.1. Men

Among men, the occurrence of frequent BNSP 4 years after follow-up was 15.3%. The crude RR for frequent BNSP among men with diabetes was 1.77 (95% CI: 1.34–2.34) compared to those men with neither diabetes nor hyperlipidaemia (Table 2). In adjusted analysis, the RR was 1.64 (95% CI: 1.23–2.18). The adjusted RR for the association between hyperlipidaemia and frequent pain was 1.19 (95% CI: 0.98–1.44). Among those who had both diabetes and hyperlipidaemia at the baseline the adjusted RR was 0.98 (95% CI: 0.65–1.47).

3.2.2. Women

The occurrence of frequent pain was 19.8% at 4 years follow-up. The crude RR for frequent pain among women with hyperlipidaemia was 1.27 (95% CI: 1.08–1.50) compared to those women with neither diabetes nor hyperlipidaemia (Table 3). After controlling for the confounders, the RR was 1.23 (95% CI: 1.03–1.46). The adjusted RR for the association between diabetes and frequent pain was 0.92 (95% CI: 0.60–1.41). Among those who had both diabetes and hyperlipidaemia at the baseline the adjusted RR was 0.96 (95% CI: 0.60–1.54).

3.3. Sensitivity analysis

Results from sensitivity analyses were in line with the ones obtained in the main analyses (Tables 4 and 5). The only difference was that a non-statistically significant increased risk of BNSP was observed among women with both diabetes and hyperlipidemia (RR = 1.34 95% CI: 0.73–2.48).

Table 1
Characteristics of the study population.

			Men		Women	
Variable	*n*	%	*n*	%	*n*	%
Sex						
Men	4384	50.6	–	–	–	–
Women	4282	49.4	–	–	–	–
Age						
45–49	1455	16.8	691	15.8	764	17.8
50–59	2941	33.9	1456	33.2	1485	34.7
60–69	2897	33.4	1528	34.9	1369	32.0
70–84	1373	15.8	709	16.2	664	15.5
BMI						
Normal or low (less than 25)	4400	50.9	1826	41.7	2574	60.3
Overweight (25–29.9)	3354	38.8	2080	47.4	1274	29.9
Obesity (30 or more)	896	10.4	478	10.9	418	9.8
Smoking habits						
Never regular smoker	3850	48.8	1907	47.7	1943	50.0
Previously daily smoker	2900	36.8	1574	39.3	1326	34.1
Current daily smoker	1140	14.4	521	13.0	619	15.9
Risky alcohol consumption	2216	27.1	1186	28.4	1030	25.8
Receiving treatment for high blood pressure	2106	24.3	1142	26.0	964	22.5
Regular physical activity	3827	44.2	1960	44.7	1867	43.6
Psychological stress	733	8.7	304	7.1	429	10.3
Socioeconomic status (occupation)						
Unskilled and semi-skilled	1008	11.6	493	11.2	515	12.0
Skilled workers	891	10.3	521	11.9	370	8.6
Assistant non-manual employees	1274	14.7	325	7.4	949	22.2
Intermediate non-manual employees	2314	26.7	1092	24.9	1222	28.5
Professionals	2206	25.5	1292	29.5	914	21.3
Self-employed non professionals	973	11.2	661	15.1	312	7.3
Diabetes/hyperlipidaemia status						
Both DM and HL	205	2.4	133	3.0	72	1.7
Only DM	246	2.8	157	3.6	89	2.1
Only HL	1142	13.2	614	14.0	528	12.3
Neither DM nor HL	7073	81.6	3480	79.4	3593	83.9
Total	8666		4384		4282	

DM: Diabetes mellitus; HL: Hyperlipidaemia; Smoking: 776 missing values (proportions based on 7890 observations); Risky alcohol intake: 499 missing values (proportions based on 8167 observations); Psychological stress: 235 missing values (proportions based on 8431 observations); Body mass index: 16 missing values (proportions based on 8650 observations).

Table 2
Relative risk (Risk Ratio) for frequent pain. Men.

Men	Crude		Adjusted[a]	
Exposure (cases/non-cases)	RR	95% CI	RR	95% CI
Neither DM nor HL (502/2978)	1		1	
Only HL (109/505)	1.23	1.02–1.49	1.19	0.98–1.44
Only DM (40/117)	1.77	1.34–2.34	1.64	1.23–2.18
Both DM and HL (21/112)	1.10	0.73–1.63	0.98	0.65–1.47

[a] Adjusted for age, body mass index, physical activity, high blood pressure and socioeconomic status; DM: Diabetes mellitus; HL: Hyperlipidemia; RR: Risk ratio; CI: Confidence interval.

Table 3
Relative risk (Risk Ratio) for frequent pain. Women.

Women	Crude		Adjusted[a]	
Exposure (cases/non-cases)	RR	95% CI	RR	95% CI
Neither DM nor HL (687/2906)	1		1	
Only HL (128/400)	1.27	1.08–1.50	1.23	1.03–1.46
Only DM (18/71)	1.06	0.70–1.61	0.92	0.60–1.41
Both DM and HL (15/57)	1.09	0.69–1.72	0.96	0.60–1.54

[a] Adjusted for age, body mass index, physical activity, high blood pressure and socioeconomic status; DM: Diabetes mellitus; HL: Hyperlipidemia; RR: Risk ratio; CI: Confidence interval.

3.4. Characterization of lost to follow-up

Information regarding the characteristics of those who answered in 2006 but did not in 2010 was collected in order to identify potential selection bias (data not shown). Of notice, the prevalence of diabetes was higher among lost to follow-up, and the prevalence of having both conditions was higher among lost to follow-up women but not among lost to follow-up men. Additionally, the prevalence of hyperlipidaemia was lower among lost to follow-up compared to the study population in both men and women. The main results are preserved, except in the extreme scenario in which it was assumed that all non-responder

Table 4
Relative risk (Risk Ratio) of frequent pain using a "stringent definition" of free from disease. Men.

Men	Crude		Adjusted[a]	
Exposure (cases/non-cases)	RR	95% CI	RR	95% CI
Neither DM nor HL (300/2401)	1		1	
Only HL (63/392)	1.25	0.97–1.61	1.17	0.90–1.52
Only DM (25/97)	1.85	1.28–2.66	1.65	1.13–2.40
Both DM and HL (10/86)	0.94	0.52–1.70	0.80	0.44–1.48

[a] Adjusted for age, body mass index, physical activity, high blood pressure and socioeconomic status; DM: Diabetes mellitus; HL: Hyperlipidemia; RR: Risk ratio; CI: Confidence interval.

Table 5
Relative risk (Risk Ratio) of frequent pain using a "stringent definition" of free from disease. Women.

Women	Crude		Adjusted[a]	
Exposure (cases/non-cases)	RR	95% CI	RR	95% CI
Neither DM nor HL (344/2216)	1		1	
Only HL (68/287)	1.43	1.13–1.80	1.40	1.10–1.79
Only DM (14/56)	1.49	0.92–2.40	1.35	0.82–2.21
Both DM and HL (9/37)	1.46	0.80–2.64	1.34	0.73–2.48

[a] Adjusted for age, body mass index, physical activity, high blood pressure and socioeconomic status; DM: Diabetes mellitus; HL: Hyperlipidemia; RR: Risk ratio; CI: Confidence interval.

women developed the outcome: in this case the association hyperlipidaemia and frequent BNSP was not statistically significant (RR = 1.06, 95% CI: 0.94–1.19).

4. Discussion

The purpose of the study was to contribute to fill the existing knowledge gap in the aetiology of BNSP through determining the effect of diabetes and hyperlipidaemia on its development. Both were shown to be independent risk factors for frequent BNSP, but having both conditions did not increase the risk in this study. The results differed to some extent between men and women: in fact among women with diabetes, no elevated risk was seen. An increased risk of frequent BNSP associated with hyperlipidaemia was observed in both men and women: however, the risk estimate was not statistically significant among men. After a sensitivity analysis, in which the cohort was restricted to those without pain or pain up to 2 days in the last 6 months, the results were similar, which is that the association between diabetes and frequent BNSP, and the one between hyperlipidaemia and frequent BNSP was preserved for men and women respectively.

Contrary to the expected, having both exposures was not associated with an increased risk of frequent BNSP in the main analysis. This may be explained by the low number of exposed cases in that category. However, another potential explanation may be that those individuals with both conditions are recommended a more intensive therapy (pharmacological and non-pharmacological) that would eventually also protect them from developing frequent BNSP.

At the sensitivity analysis using a more stringent definition of free from pain, women, but not men, showed important variation (increase) in the risk for all exposures, although not reaching statistical significance, except for hyperlipidaemia. These results may suggest differences in the course of frequent pain by sex: for women, reporting pain a couple of days in the last month (intermediate category according to the response options in the 2006 questionnaire) are more likely to progress towards developing more frequent BNSP rather than going back to the category "free from the disease"; and the opposite for men.

The present study is in line with two previous longitudinal studies. In a Finnish cohort study with a 28 years follow-up period, cholesterol but not triglycerides were associated with incident local low back pain after adjusting for significant confounders [23]. Unlike that study, ours presents RR based on a dichotomized outcome, instead of comparing different tertiles. Similarly, in another study from Finland, cholesterol was associated with higher probability of occlusion of lumbar arteries, which according to the author, can lead to disc degeneration, which thereafter could lead to back pain [34].

On the contrary, a Norwegian cohort with 11 year follow-up examining lipids and low back pain, stratified by sex, showed no results for onset of pain in the adjusted models [35]. It is possible that the null findings were explained by the prolonged follow-up time in that study and because of pain may change over time. Additionally, the authors suggest that their positive findings in the crude analysis were in fact explained by BMI, while in the current study adjusting for BMI did not have any impact on the association between hyperlipidaemia and frequent BNSP among women.

Our results, in terms of occurrence of frequent BNSP and the effect of diabetes, differ by sex. If biological differences in terms of either tissue composition or metabolic activity by sex are considered, this result is not surprising and on the other hand, a distinct behaviour between men and women can contribute to explain the result; for example, women may follow lifestyle recommendations to a greater extent than men. The role of other external factors such as differences in the filling of the questionnaire cannot be excluded.

Previous studies have also shown differential results by sex, for example, another report from the above-mentioned Finnish group that compared seven cardiovascular risk factors, among them triglycerides and cholesterol, with frequent radiating pain in the back during the past 12 months, in which serum triglycerides showed a statistically significant odds ratio (OR) of 2.28 in men but not in women [22]. Differences in the follow-up time as well as the period measured (12 months instead of six) may be an explanation for the discrepant results with respect to the present results in addition to the fact that OR tends to overestimate the associations compared to risk ratio, given that the outcome is relatively common.

This study was a 4 year follow up cohort were information from a random sample of the population was collected. This makes it possible to generalize the results to a broader population compared to studies based on individuals attending specialized clinics or with specific diagnosis. Furthermore, the questionnaire was translated into six foreign languages and various attempts were done in order to reach a more representative sample of the individuals living in Stockholm, which reduce the risk of selection bias. A

potential selection bias was evaluated by simulating extreme scenarios (that either all or none of the lost to follow-up develop the outcome) based on the information on lost individuals, being found that the main results of this study are preserved. The stratification by sex made it possible to study potential differences between men and women. Despite a large study population, due to the low prevalence of diabetes mellitus we did not have enough power to detect modest associations, especially among individuals who had both conditions: only 21 men and 15 women with both conditions reported frequent BNSP.

The data was self-reported, which would increase the risk of non-differential misclassification of diabetic individuals as non-diabetic, and therefore, a dilution of the effect would occur; however, given the relatively high sensitivity and specificity of the self-reported data reported in previous studies [36], the magnitude of such dilution would be marginal. Concerning hyperlipidaemia, a more careful analysis should be done since it was not specified which component of the lipid profile (triglycerides, total cholesterol or low density lipoprotein) was elevated and the validity of self-reported data here is less good than in diabetes [36].

A consideration should be made concerning the way the exposures were asked in the 2006 questionnaire ("*Have you received any or some of the following diagnoses by a doctor*?"): diabetes is a quite stable diagnosis, and usually requires confirmation by further tests, but contrarily, hyperlipidaemia is more often a reversible condition [37] and therefore, patients could have had such diagnosis before, but being free from it at the moment of the survey and during the follow-up. On the other hand, given the fact that women usually attend the healthcare services more often than men [38], it could be hypothesized that men who received these diagnoses (diabetes and hyperlipidaemia) were more severe cases and that would be the reason why the association for diabetes and frequent BNSP was clearer among men than among women. Furthermore, the term "diabetes" may refer to type 1 diabetes mellitus or to type 2 diabetes mellitus. It is not possible to report, based on this study, whether a potential association between DM and frequent BNSP is more due to one type or the other. But since type 2 diabetes mellitus is the dominant type of diabetes, it is more likely that the results are depending on this type of diabetes.

Statins have been studied in cross-sectional studies and found to be associated with musculoskeletal pain [39], thus may explain the findings concerning hyperlipidaemia and our outcome. Statins may, however, lie in the causal pathway of the association between hyperlipidaemia and BNSP, and should as such not be controlled for, but rather stratified for. We did unfortunately not have any information about medicine use, thus could not assess the role of statins.

Residual or unmeasured confounding may also be a limitation in the study, but overall, we believe that the role of unmeasured confounders is most likely to be marginal.

A last, but not least consideration is regarding the duration of the follow-up. Information on episodes of pain during the first three and a half years of follow-up was lacking, as well as whether some individuals, regardless of the exposure, got therapies for such episodes of pain and were free from them at the time of the follow-up. Since the exact mechanism of the – potential – association is not yet clarified, it is not known whether a shorter or longer follow-up would give different results. We have no reason to believe though that this potential misclassification of exposure differ between exposed and un-exposed.

Risk factors for BNSP have been studied extensively, but it is also important to discuss the contribution of each risk factor for the development of an outcome. To illustrate this in our study, we calculated the population-attributable fraction for diabetes among men – which is, the reduction in incidence of the outcome if the exposure was removed from the population. [33] It is approximately 6%, which means that this exposure only contributes to a small fraction to the onset of BNSP. If diabetes increases in the population, which is the case globally, it also means that the incidence of BNSP may increase.

Further research investigating the combined effect of the exposures is needed to clarify the associations studied here, as well as more stringent measurement of the outcome. Future longitudinal studies may ensure a better measurement of metabolic conditions using laboratory tests, as well as a more comprehensive way of measuring musculoskeletal pain and disability. Additionally, such research should consider more than one cut-off point in time in order to obtain a better description of the course of the outcome in relation to the exposures.

5. Conclusions

This study suggests that metabolic diseases such as diabetes and hyperlipidaemia may have an impact on the pathophysiology of frequent BNSP. To conclude, there was a higher risk of frequent BNSP among individuals with diabetes mellitus or hyperlipidaemia. For diabetes mellitus, the risk may differ to some extent by sex, being present in men only. A combination of the two exposures did not increase the risk of frequent BNSP in any of the sexes.

6. Implications

Health professionals should contemplate the results from this study when planning primary prevention strategies.

Ethical issues

All the participants were informed of the purpose of the research and gave their informed consent to the preservation of their national registration number, future contacts and record linkages [37]. There is an ethical approval for this study (DNr: 2013/497-32) and the Stockholm Public Health Cohort Steering Committee reviewed the present proposal prior to the provision of the data. There is no conflict of interest declared by the authors.

Conflict of interest

The authors declare that they do not have any conflict of interest to this paper.

Acknowledgments

The Stockholm Public Health Cohort was financed by Stockholm County Council.

Oscar Javier Pico Espinosa received financial support from the Swedish Institute during the period in which this research was conducted.

References

[1] Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386:743–800, http://dx.doi.org/10.1016/S0140-6736(15)60692-4.

[2] Hoy D, March L, Woolf A, Blyth F, Brooks P, Smith E, Vos T, Barendregt J, Blore J, Murray C, Burstein R, Buchbinder R. The global burden of neck pain: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis 2014;73:1309–15, http://dx.doi.org/10.1136/annrheumdis-2013-204431.

[3] Skillgate E, Magnusson C, Lundberg M, Hallqvist J. The age- and sex-specific occurrence of bothersome neck pain in the general population – results from the Stockholm public health cohort. BMC Musculoskelet Disord 2012;13:185, http://dx.doi.org/10.1186/1471-2474-13-185.

[4] Strine TW, Hootman JM. US national prevalence and correlates of low back and neck pain among adults. Arthritis Rheum 2007;57:656–65, http://dx.doi.org/10.1002/art.22684.
[5] Ha IH, Lee J, Kim MR, Kim H, Shin JS. The association between the history of cardiovascular diseases and chronic low back pain in South Koreans: a cross-sectional study. PLoS One 2014;9:e93671, http://dx.doi.org/10.1371/journal.pone.0093671.
[6] Dean BJF, Gwilym SE, Carr AJ. Why does my shoulder hurt? A review of the neuroanatomical and biochemical basis of shoulder pain. Br J Sports Med 2013;47:1095–104, http://dx.doi.org/10.1136/bjsports-2012-091492.
[7] Seaman DR, Cleveland C. Spinal pain syndromes: nociceptive, neuropathic, and psychologic mechanisms. J Manipulative Physiol Ther 1999;22:458–72.
[8] Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL. Sex, gender, pain: a review of recent clinical and experimental findings. J Pain 2009;10:447–85, http://dx.doi.org/10.1016/j.jpain.2008.12.001.
[9] Bohman T, Alfredsson L, Jensen I, Hallqvist J, Vingård E, Skillgate E. Does a healthy lifestyle behaviour influence the prognosis of low back pain among men and women in a general population? A population-based cohort study. BMJ Open 2014;4:e005713, http://dx.doi.org/10.1136/bmjopen-2014-005713.
[10] McLean SM, May S, Klaber-Moffett J, Sharp DM, Gardiner E. Risk factors for the onset of non-specific neck pain: a systematic review. J Epidemiol Community Health 2010;64:565–72, http://dx.doi.org/10.1136/jech.2009.090720.
[11] Kane S, Conus S, Haltom D, Hirshorn K, Pak Y, Vigdorchik J. A shoulder health survey: correlating behaviors and comorbidities with shoulder problems. Sports Health 2010;2:119–34, http://dx.doi.org/10.1177/1941738109338358.
[12] Hogg-Johnson S, van der Velde G, Carroll LJ, Holm LW, Cassidy JD, Guzman J, Coté P, Haldeman S, Ammendolia C, Carragee E, Hurwitz E, Nordin M, Peloso P. The burden and determinants of neck pain in the general population. Results of the bone and joint decade 2000–2010 task force on neck pain and its associated disorders. J Manipulative Physiol Ther 2009;2:s46–60, http://dx.doi.org/10.1016/j.jmpt.2008.11.010.
[13] Paanalahti K, Holm LW, Magnusson C, Carroll L, Nordin M, Skillgate E. The sex-specific interrelationship between spinal pain and psychological distress across time in the general population. Results from the Stockholm Public Health Study. Spine J 2014;14:1928–35, http://dx.doi.org/10.1016/j.spinee.2013.11.017.
[14] Pinheiro MB, Ferreira ML, Refshauge K, Ordo JR, Machado GC, Prado LR, Maher CG, Ferreira PH. Symptoms of depression and risk of new episodes of low back pain: a systematic review and meta-analysis. Arthritis Care Res 2015;67:1591–603, http://dx.doi.org/10.1002/acr.22619.
[15] Bohman T, Alfredsson L, Hallqvist J, Vingård E, Skillgate E. The influence of self-reported leisure time physical activity and the body mass index on recovery from persistent back pain among men and women: a population-based cohort study. BMC Public Health 2013;13:385, http://dx.doi.org/10.1186/1471-2458-13-385.
[16] Rasmussen-Barr E, Bohman T, Hallqvist J, Holm LW, Skillgate E. Do physical activity level and body mass index predict recovery from persistent neck pain in men and women of working age? A population-based cohort study. Eur Spine J 2013;22:2077–83, http://dx.doi.org/10.1007/s00586-013-2801-x.
[17] Palmlöf L, Skillgate E, Alfredsson L, Vingård E, Magnusson C, Lundberg M, Holm LW. Does income matter for troublesome neck pain? A population-based study on risk and prognosis. J Epidemiol Community Health 2012;66:1063–70, http://dx.doi.org/10.1136/jech-2011-200783.
[18] Hurwitz EL, Carragee EJ, van der Velde G, Carroll LJ, Nordin M, Guzman J, Peloso PM, Holm LW, Coté P, Hogg-Johnson S, Cassidy JD, Haldeman S. Treatment of neck pain: noninvasive interventions. Results of the bone and joint decade 2000–2010 task force on neck pain and its associated disorders. J Manipulative Physiol Ther 2009;32:123–52, http://dx.doi.org/10.1016/j.jmpt.2008.11.017.
[19] Mäntyselkä P, Miettola J, Niskanen L, Kumpusalo E. Chronic pain, impaired glucose tolerance and diabetes: a community-based study. Pain 2008;2:s46–60, http://dx.doi.org/10.1016/j.pain.2007.08.007.
[20] Molsted S, Tribler J, Snorgaard O. Musculoskeletal pain in patients with type 2 diabetes. Diabetes Res Clin Pract 2012;96:135–40, http://dx.doi.org/10.1016/j.diabres.2011.12.022.
[21] Ramchurn N, Mashamba C, Leitch E, Arutchelvam V, Narayanan K, Weaver J, Hamilton J, Heycock C, Saravanan V, Kelly C. Upper limb musculoskeletal abnormalities and poor metabolic control in diabetes. Eur J Intern Med 2009;20:718–21, http://dx.doi.org/10.1016/j.ejim.2009.08.001.
[22] Leino-Arjas P, Solovieva S, Kirjonen J, Reunanen A, Riihimäki H. Cardiovascular risk factors and low-back pain in a long-term follow-up of industrial employees. Scand J Work Environ Health 2015;32:12–9.
[23] Leino-Arjas P, Kaila-Kangas L, Solovieva S, Riihimäki H, Kirjonen J, Reunanen A. Serum lipids and low back pain: an association? A follow-up study of a working population sample. Spine (Phila Pa 1976) 2006;31:1032–7, http://dx.doi.org/10.1097/01.brs.0000214889.31505.08.
[24] Fields AJ, Berg-Johansen B, Metz LN, Miller S, La B, Liebenberg EC, Coughlin DG, Graham JL, Stanhope KL, Havel PJ, Lotz JC. Alterations in intervertebral disc composition, matrix homeostasis and biomechanical behavior in the UCD-T2DM rat model of type 2 diabetes HHS Public Access. J Orthop Res 2015;33:738–46, http://dx.doi.org/10.1002/jor.22807.
[25] Tsai T-T, Yi-Ju Ho N, Lin Y-T, Lai P-L, Fu T-S, Niu C-C, Chen L-H, Chen W-J, Pang J-HS. Advanced glycation end products in degenerative nucleus pulposus with diabetes. J Orthop Res 2014;32:238–44.
[26] Deleo JA, Winkelstein BA. Physiology of chronic spinal pain syndromes from animal models to biomechanics. Spine (Phila Pa 1976) 2002;27:2526–37, http://dx.doi.org/10.1097/01.BRS.0000032126.97065.FE.
[27] Cruz NG, Sousa LP, Sousa MO, Pietrani NT, Fernandes AP, Gomes KB. The linkage between inflammation and Type 2 diabetes mellitus. Diabetes Res Clin Pract 2013;99:85–92, http://dx.doi.org/10.1016/j.diabres.2012.09.003.
[28] Siasos G, Tousoulis D, Oikonomou E, Zaromitidou M, Stefanadis C, Papavassiliou AG. Inflammatory markers in hyperlipidemia: from experimental models to clinical practice. Curr Pharm Des 2011;17:4132–46.
[29] Svensson AC, Fredlund P, Laflamme L, Hallqvist J, Alfredsson L, Ekbom A, Feychting M, Forsberg B, Pedersen NL, Vågerö D, Magnusson C. Cohort profile: the Stockholm public health cohort. Int J Epidemiol 2013;42:1263–72, http://dx.doi.org/10.1093/ije/dys126.
[30] Benfeldt C, Vibeke B. Teknisk rapport. Stockholm: Hälsa Stockholm; 2014. p. 339.
[31] Andreason S, Allebeck P. Alkohol och hälsa. Stockholm: Statens Folkhälsoinstitut; 2005. p. 98.
[32] Goldberg DP, Gater R, Sartorius N, Ustun TB, Piccinelli M, Gureje O, Rutter C. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. Psychol Med 1997;27:191–7.
[33] Rothman K, Greenland S. Modern epidemiology. 2nd ed. Philadelphia: Lippincott – Raven; 1998.
[34] Kauppila LI, Mikkonen R, Mankinen P, Pelto-Vasenius K, Mäenpää I. MR aortography and serum cholesterol levels in patients with long-term nonspecific lower back pain. Spine (Phila Pa 1976) 2004;29:2147–52.
[35] Heuch I, Heuch I, Hagen K, Zwart J-A. Do abnormal serum lipid levels increase the risk of chronic low back pain? The Nord-Trøndelag Health Study. PLoS One 2014;9:e108227, http://dx.doi.org/10.1371/journal.pone.0108227.
[36] Bowlin SJ, Morrill BD, Nafziger AN, Lewis C, Pearson TA. Reliability and changes in validity of self-reported cardiovascular disease risk factors using dual response: the behavioral risk factor survey. J Clin Epidemiol 1996;49:511–7.
[37] Cholesterol Treatment Triallist Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. Lancet 2010;376:1670–81, http://dx.doi.org/10.1016/S0140-6736(10)61350-5.
[38] Osika Friberg I, Krantz G, Maatta S, Jarbrink K. Sex differences in health care consumption in Sweden: a register-based cross-sectional study. Scand J Public Health 2016;44:264–73, http://dx.doi.org/10.1177/1403494815618843.
[39] Buettner C, Rippberger MJ, Smith JK, Leveille SG, Davis RB, Mittleman MA. Statin use and musculoskeletal pain among adults with and without arthritis. Am J Med 2012;125:176–82, http://dx.doi.org/10.1016/j.amjmed.2011.08.007.