

# Socioeconomic status and esophageal squamous cell carcinoma risk in Kashmir, India

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Studies have persistently associated esophageal squamous cell carcinoma (ESCC) risk with low socioeconomic status (SES), but this association is unexplored in Kashmir, an area with a high incidence of ESCC in the northernmost part of India. We carried out a case-control study to assess the association of multiple indicators of SES and ESCC risk in the Kashmir valley. A total number of 703 histologically confirmed ESCC cases and 1664 controls matched to the cases for age, sex, and district of residence were recruited from October 2008 to January 2012. Conditional logistic regression models were used to calculate unadjusted and adjusted odds ratios and 95% confidence intervals. Composite wealth scores were constructed based on the ownership of several appliances using multiple correspondence analyses. Higher education, living in a kiln brick or concrete house, use of liquefied petroleum gas and electricity for cooking, and higher wealth scores all showed an inverse association with ESCC risk. Compared to farmers, individuals who had government jobs or worked in the business sector were at lower risk of ESCC, but this association disappeared in fully adjusted models. Occupational strenuous physical activity was strongly associated with ESCC risk. In summary, we found a strong relationship of low SES and ESCC in Kashmir. The findings need to be studied further to understand the mechanisms through which such SES parameters increase ESCC risk. (*Cancer Sci* 2013; 104: 1231–1236)

Esophageal cancer is the sixth most common cause of cancer deaths in the world,<sup>(1)</sup> but approximately 83% of its incident cases and 86% of deaths occur in developing countries.<sup>(1)</sup> There are two main forms of esophageal cancer, squamous cell carcinoma and adenocarcinoma.<sup>(2)</sup> Esophageal squamous cell carcinoma is the most common histological type of esophageal cancer globally<sup>(3)</sup> and constitutes 90% of cases in the high-risk region in Central Asia, often referred to as the “esophageal cancer belt”.<sup>(3–5)</sup> Because of the high incidence and poor prognosis, ESCC contributes significantly to the cancer burden in the belt and some other high-incidence countries.<sup>(6)</sup> However, the etiology of ESCC is yet an open question in these areas.

Studies have reported an association between low SES and ESCC.<sup>(5,7–12)</sup> Although low SES is not a biological cause of cancer, it may influence the risk through behavior, lifestyle, environmental exposure, and diet. Low SES may also be a measure of access to the basic resources required to achieve and maintain good health.<sup>(13)</sup>

ESCC is the most common cancer in Kashmir,<sup>(14,15)</sup> a part of northern most India and the Asian esophageal cancer belt. Although the SES of the population in the region is generally low,<sup>(16)</sup> no study from Kashmir has investigated in detail the association between low SES and ESCC. Hence, we carried

out a case-control study to examine this association. Many factors, including income, profession, housing, and education can determine SES.<sup>(17)</sup> Therefore, as recommended in previous reports,<sup>(18,19)</sup> we selected a wide range of potential SES indicators in order to assess SES in this study.

## Materials and Methods

**Case and control selection.** Details of the study methods are described elsewhere.<sup>(20)</sup> Briefly, all ESCC cases were recruited in the Oncology Department of SKIMS (Srinagar, India) from October 2008 to January 2012. Histopathological confirmation for ESCC, age older than 18 years, and no history of previous cancer were the other inclusion criteria for cases.

For each case subject, we recruited at least one hospital-based control individually matched to the case for sex, age ( $\pm 5$  years), and district of residence from inpatient wards of SKIMS and other hospitals. Patients were enrolled as controls only when the disease for which they had been admitted was not strongly associated with tobacco or alcohol consumption, based on previous published reports. The reasons for hospitalization of controls are shown in Table S1. The controls were recruited within 6 months after their respective cases were recruited. The participation rate for cases and control was 96% (732 invited, 29 refusals) and 98% (1697 invited, 33 refusals), respectively. The majority of those who refused were too ill to participate in the study. For most of the cases (91%), there were two (for 377 cases) or three controls (for 268 cases). We were able to recruit only one control for 44 cases and more than three controls for 14 cases. Informed consent was obtained from all subjects. This study was reviewed and approved by the Institutional Ethics Committee of SKIMS.

**Data collection.** Interviews with ESCC cases were carried out at SKIMS. Controls were interviewed at the hospitals in which they were recruited. Data on SES indicators and potential confounding factors of interest, such as smoking and smokeless tobacco, alcohol use, and fresh fruit and vegetable intake, were collected. In order to minimize interindividual variation, a limited number of staff carried out the face-to-face interviews, using structured questionnaires, and no proxies were used.

The potential parameters of SES for which information was obtained were education level (highest level attained), occupation, professional work intensity, income, house type, cooking fuel, place of residence, and ownership of several household appliances, including personal automobile, motorbike, B/W TV, color TV, refrigerator, washing machine, vacuum cleaner, computer, and bath in the residence. Subjects of different

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professions were grouped into farmers, unskilled and skilled workers, household workers (engaged in work in their own houses and were not employed outside the home), government employees, and people in the business sector. Professional physical activities were categorized into sedentary (clerk, accountant, engineer, indoor works), active (barber, academic teacher, policeman, mechanic), and very active (farmer, brick or stone setter, landscape worker, logger, construction workers).

**Statistical analysis.** Numbers and percentages were calculated and presented for various demographic and SES categorical variables. Similar to an earlier study on SES and esophageal cancer in Golestan Province, Iran, an area with high incidence of ESCC in a middle-income country,<sup>(7)</sup> we built a composite score for wealth based on ownership of appliances, and other variables. We used MCA on personal car, motorbike, B/W TV, color TV, refrigerator, freezer, vacuum cleaner, washing machine, and computer ownership variables, as well as having a bath in the residence. The scores were calculated and categorized as quintiles according to the observed coordinates among control subjects. Information on the MCA method is provided in Data S1.

Conditional logistic regression was used to calculate unadjusted and adjusted ORs and corresponding 95% CIs for each SES parameter. Fruit and vegetable intake data (g/day) were transformed to logarithmic values following addition of 0.1 to original values. By design, case and control subjects were matched by age, sex, and district of residence. Adjusted ORs (95% CIs) were obtained from two models. In the first model, ORs (95% CIs) were adjusted for demographic factors, including age, ethnicity, place of residence (rural/urban), religion, and education level. Age was included in the multivariate models, because the matching for age was not perfect ( $\pm 5$  years). We adjusted the results for religion because an earlier study from this region had suggested dissimilar incidence of ESCC among people with different religions.<sup>(21)</sup> As several of the SES indicators in this study, including occupation, monthly income, house type, cooking fuel, and wealth score, usually related strongly to economic status, they were not adjusted for each other. However, as education level may capture some aspects of SES other than economic status,<sup>(7)</sup> the results for all these variables were adjusted for education. Results for education were adjusted for the wealth score and not for other indicators of economic status. In the second group of models, in addition to these demographic factors, some biologic factors, including daily fresh fruit and vegetable intake (logarithmic scale), cumulative use of cigarettes, hookah, and nass, and ever-use of bidi, gutka, and alcohol, were included one by one and then collectively.

All statistical analyses were carried out using STATA software, version 12 (Stata, College Station, TX, USA). Two sided *P*-values < 0.05 were considered statistically significant.

## Results

A total of 703 ESCC cases and 1664 matched controls were recruited in this study. Distribution of demographic factors and tobacco and alcohol use by case status are shown in Table 1. The mean age of cases and controls was 61.6 and 59.8 years, respectively. Approximately 55% of cases and controls were males. The majority of participants (~97%) were of the Kashmiri ethnic group. More than 90% of the subjects were from rural areas. Fresh fruit and vegetable intake among controls was higher than in cases, but hookah, bidi, nass, and gutka use was more frequent in cases.

The association between potential SES indicators and ESCC risk are shown in Tables 2 and S2. Results in Table S2 are adjusted for demographic factors, as well as one of

**Table 1. Characteristics of 703 esophageal squamous cell carcinoma cases and 1664 controls from Kashmir Valley, India, 2008–2012†**

Characteristics	Cases (%)	Controls (%)	<i>P</i> -value
Age, years, mean (SD)	61.6 (11.1)	59.8 (11.1)	
Sex			
Male	393 (55.9)	920 (55.3)	0.780
Female	310 (44.1)	744 (44.7)	
Place of residence			
Urban	29 (4.1)	146 (8.8)	<0.001
Rural	674 (95.9)	1518 (91.2)	
Ethnicity			
Kashmiri	682 (97.0)	1619 (97.3)	0.580
Gojri	11 (1.6)	16 (1.0)	
Pahari	9 (1.3)	27 (1.6)	
Other	1 (0.1)	2 (0.1)	
Religion			
Muslim	695 (98.9)	1648 (99.0)	0.030
Hindu	5 (0.7)	2 (0.1)	
Sikh	3 (0.4)	14 (0.8)	
Fresh fruit and vegetable intake, median g/day (IQR)	7.9 (3.8–12.6)	25.2 (12.0–60.9)	<0.001
Hookah smoking, hookah-years			
Never	282 (40.2)	964 (58.0)	<0.001
1–139	97 (13.8)	228 (13.7)	
140–240	110 (15.7)	245 (14.8)	
>240	213 (30.3)	224 (13.5)	
Cigarette smoking, pack-years			
Never	632 (90.0)	1437 (86.4)	0.010
1–6.2	23 (3.3)	77 (4.6)	
6.3–13.1	21 (3.0)	73 (4.4)	
≥13.2	26 (3.7)	76 (4.6)	
Bidi ever smoking	15 (2.1)	3 (0.2)	<0.001
Nass chewing, nass-years			
Never	501 (71.6)	1471 (88.5)	<0.001
1–119	46 (5.6)	52 (3.1)	
120–199	36 (5.1)	71 (4.3)	
≥200	117 (16.7)	69 (4.1)	
Gutka ever chewing	10 (1.4)	13 (0.8)	0.010
Alcohol ever use	8 (1.1)	0 (0.0)	<0.001

†Although cases and controls were individually matched, the percentages of cases and controls are not necessarily equal in each sex category, because some cases have one matched control and others have more than one matched control. Numbers may not add up to the total numbers due to missing data in some variables. *P*-values calculated using  $\chi^2$ -tests for categorical variables ( $\chi^2$  for trend in variables with more than two categories) and Wilcoxon rank sum tests for continuous variables. IQR, inter-quartile range.

the following potential biologic risk factors of ESCC: daily fresh fruit and vegetable intake; and cumulative use of cigarettes, hookah, and nass. Table 2 shows the unadjusted results, results adjusted for demographic factors only, and fully adjusted results (including demographic and biologic factors). There was an inverse association between education level and ESCC, which was significant for all education levels, including primary school (OR = 0.29; 95% CI, 0.17–0.49). Compared to farmers, there was an inverse association between working in government jobs or in the business sector, but these associations disappeared after adjustments for other factors. Adjustment for fresh fruit and vegetable intake was the main reason for the difference between unadjusted and fully adjusted models. When compared to sedentary jobs, the risk was higher for active jobs (OR = 3.07; 95% CI, 2.13–4.40) and very active jobs (OR = 5.65, 95% CI, 3.49–9.12). Monthly income also showed an inverse association

**Table 2. Association between indicators of socioeconomic status and esophageal squamous cell carcinoma risk, Kashmir Valley, India, 2008–2012**

Socioeconomic parameters	Cases (%)	Controls (%)	Unadjusted OR (95% CI)†	Adjusted OR (95% CI)‡	Adjusted OR (95% CI)§
<b>Education</b>					
No school	626 (89.0)	1074 (64.5)	Referent	Referent	Referent
Primary (<5th)	33 (4.7)	203 (12.2)	0.22 (0.15–0.33)	0.21 (0.14–0.34)	0.29 (0.17–0.49)
Middle (5th–8th)	24 (3.4)	123 (7.4)	0.26 (0.16–0.42)	0.28 (0.17–0.47)	0.39 (0.20–0.73)
High school (9th–12th)	16 (2.3)	149 (9.0)	0.14 (0.08–0.25)	0.17 (0.09–0.30)	0.42 (0.19–0.89)
Graduates and higher	4 (0.6)	115 (6.9)	0.05 (0.02–0.14)	0.05 (0.02–0.13)	0.19 (0.06–0.60)
<i>P</i> for trend			<0.001	<0.001	<0.001
<b>Occupation</b>					
Farming	278 (39.5)	569 (34.2)	Referent	Referent	Referent
Unskilled work	68 (9.7)	116 (6.9)	1.06 (0.75–1.51)	1.29 (0.88–1.92)	1.25 (0.75–2.09)
Skilled work	48 (6.8)	83 (5.0)	1.06 (0.70–1.59)	1.43 (0.89–2.28)	1.86 (1.04–3.35)
House work	266 (37.8)	611 (36.7)	1.23 (0.86–1.77)	1.22 (0.83–1.80)	1.16 (0.71–1.88)
Government job	37 (5.3)	240 (14.4)	0.28 (0.19–0.42)	0.75 (0.46–1.23)	0.85 (0.46–1.56)
Business	6 (0.9)	45 (2.7)	0.27 (0.11–0.64)	0.65 (0.24–1.73)	0.90 (0.28–2.85)
<b>Occupational physical activity</b>					
Sedentary	83 (11.8)	594 (35.7)	Referent	Referent	Referent
Active	453 (66.4)	912 (54.8)	4.05 (3.05–5.38)	3.34 (2.47–4.52)	3.07 (2.13–4.40)
Very active	167 (23.8)	157 (9.5)	9.52 (6.60–3.71)	6.64 (4.45–9.91)	5.65 (3.49–9.12)
<i>P</i> for trend			<0.001	<0.001	<0.001
<b>Monthly income (Indian Rupee)</b>					
≤ 5000	514 (77.0)	988 (59.5)	Referent	Referent	Referent
5001–10 000	102 (14.5)	384 (23.1)	0.50 (0.39–0.64)	0.57 (0.44–0.74)	0.76 (0.55–1.04)
> 10 000	60 (8.5)	290 (17.4)	0.36 (0.26–0.49)	0.72 (0.50–1.05)	0.99 (0.63–1.56)
<i>P</i> for trend			<0.001	0.001	0.001
<b>House type</b>					
Adobe	432 (61.5)	413 (24.8)	Referent	Referent	Referent
Kiln brick	195 (27.7)	1001 (60.2)	0.17 (0.14–0.21)	0.20 (0.16–0.26)	0.20 (0.15–0.27)
Concrete	76 (10.8)	250 (15.0)	0.27 (0.19–0.37)	0.38 (0.27–0.55)	0.45 (0.29–0.70)
<b>Cooking fuel</b>					
Animal dung, wood, biomass	685 (97.7)	1358 (82.0)	Referent	Referent	Referent
Electricity	3 (0.4)	32 (1.9)	0.18 (0.54–0.60)	0.18 (0.05–0.65)	0.24 (0.05–1.20)
Gas	13 (1.9)	266 (16.1)	0.08 (0.04–0.14)	0.80 (0.40–0.15)	0.10 (0.05–0.19)
<b>Wealth score</b>					
Quintile 1 – lowest	399 (56.8)	335 (20.1)	Referent	Referent	Referent
Quintile 2	109 (15.5)	331 (19.9)	0.29 (0.22–0.38)	0.29 (0.22–0.39)	0.40 (0.28–0.57)
Quintile 3	67 (9.5)	333 (20.0)	0.15 (0.11–0.21)	0.16 (0.11–0.23)	0.16 (0.10–0.24)
Quintile 4	70 (10.0)	333 (20.0)	0.15 (0.10–0.20)	0.19 (0.14–0.28)	0.27(0.18–0.41)
Quintile 5	58 (8.2)	332 (20.0)	0.12 (0.08–0.17)	0.20 (0.13–0.23)	0.29 (0.18–0.46)
<i>P</i> for trend			<0.001	<0.001	<0.001

Numbers may not add up to the total numbers due to missing data in some variables. †By design, controls were individually matched to cases for age, sex, and district of residence. ‡Adjusted for age, ethnicity, place of residence, religion, and education. §Adjusted for age, ethnicity, place of residence, religion, daily fresh fruit and vegetable intake (logarithmic scale), cumulative use of cigarettes, hookah, and nass, and ever-use of bidi, gutka, and alcohol. Results for education were additionally adjusted for the wealth score. Results for other variables in the table were additionally adjusted for education.

with ESCC in unadjusted models (*P* for trend <0.001). In adjusted models, this association persisted only for monthly income up to 10 000 Indian Rupees. Living in houses that were made of kiln burnt brick and concrete showed inverse association when compared with subjects living in adobe-made houses. Using electricity (OR = 0.24; 95% CI, 0.05–1.20) and LPG (OR = 0.10; 95% CI, 0.05–0.19) as cooking fuel was associated with lower ESCC risk than less expensive and easily available fuels in the region, including animal dung, fire wood, and biomass.

The wealth score also showed an inverse association with ESCC risk, the ORs for quintiles 2 to 5 in adjusted models were not substantially different. When analyzed individually, ownerships of all appliances were inversely associated with ESCC risk in unadjusted models (Table S3). The association of ESCC with ownership of refrigerator, computer, motorbike, and car disappeared after adjustments for other factors.

Cigarette smoking was more common in people with higher education and higher wealth score. In contrast, hookah and nass use was more common among those with lower education levels and wealth score (Table S4).

## Discussion

Our study showed association between indicators of low SES and ESCC risk in Kashmir. Formal education and appliance ownership-based wealth score, as well as living in certain house structures and using certain cooking fuels that reflected higher economic status in Kashmir valley, were inversely associated with ESCC risk.

Education has been consistently used as a marker of SES and is inversely associated with risk of ESCC.<sup>(7,8,22,23)</sup> In general, information on education level is relatively easy to collect from study subjects and is unlikely to be affected by recall



bias. Also, as education level is unlikely to change in adulthood, it is not influenced by health status in old age. Higher education may also reflect higher SES of a family during childhood, which may have an effect on future health. In addition, people with higher education may be more likely to get well-paid jobs<sup>(24)</sup> and obtain health-related knowledge, which may modulate cancer risk.<sup>(19)</sup>

Government jobs and business professions showed an inverse relationship with ESCC risk in unadjusted analyses. People with these jobs had higher income and education levels, on average, than other individuals. Disappearance of the above associations following adjustments for fruit and vegetable intake suggests that nutritional factors were the main reasons for observing inverse associations between these jobs and the ESCC risk.

Previous epidemiologic data concerning the relationship between physical activity and esophageal cancer are inconclusive and show mixed results.<sup>(25–30)</sup> Studies have reported inverse,<sup>(27,28)</sup> suggestive of inverse,<sup>(29)</sup> or no association<sup>(25,30)</sup> between physical activity and risk of esophageal adenocarcinoma. Data on the association between physical activity and ESCC are more limited. One study<sup>(26)</sup> has reported no association, whereas another study reported an association between less professional physical activity and an increased risk of ESCC in women only.<sup>(31)</sup> In the current study, the risk of ESCC increased as the level of professional physical activity increased. People working in jobs demanding strenuous physical activity were more likely to have lower SES. Although we adjusted the results for several SES indicators, this association may be related to residual confounding from SES or some unknown biological reason. Further studies are needed to understand the association between strenuous professional activity and esophageal cancer in people with low SES.

In this study, living in kiln brick and concrete houses as compared to living in adobe houses was associated with a lower ESCC risk. House type is an economic marker to identify low-income people and to ensure better targeting of developmental programs,<sup>(32)</sup> and is frequently used in statistical, economic, and census surveys by government agencies to measure SES in India.<sup>(33)</sup> The order of house types that represent economic status (from lower to higher) in India is: (i) adobe (*kachcha*); (ii) kiln burnt brick house (*semi-pukka*); and (iii) concrete house (*pukka*).<sup>(34)</sup> The Hindi word *kachcha* is associated with poverty and backwardness, whereas *pukka* is associated with progress and modernity. Adobe building is made up of unprocessed natural material such as mud, thatch, and wood available in the vicinity and the cost of construction is minimal. Concrete buildings are built from industrially produced construction materials like brick, stone, tile, metal, and mortar.<sup>(35)</sup> Kiln burnt brick buildings are a representation of intermediary economic status of the population.

The use of more expensive fuels for cooking was associated with a lower ESCC risk in this study. In fact, the economic position is the main determinant in choosing a fuel for cooking in India. Over 85% of rural and 20% of urban Indians use cow dung, firewood, kerosene, and biomass as the primary source of fuel for cooking.<sup>(36)</sup> Even in urban India, the proportion of those using LPG is under two-thirds.<sup>(36)</sup> The ranking of options from low to high cost is firewood, cow dung, and biomass to LPG and electricity.<sup>(37)</sup> Therefore, people with higher SES are more likely to use LPG and electricity for cooking and heating, whereas people with lower SES are more likely to use fuels like animal dung, wood, and biomass,<sup>(38)</sup> which in many cases are byproducts of their agricultural activities. The energy ladder model (reviewed in Heltberg, 2004)<sup>(39)</sup> argues that the three-stage fuel switching process from basic biomass (1st level) to kerosene, coal, and charcoal (2nd transition level), and to LPG, natural gas, or elec-

tricity (3rd level) is income and fuel price driven.<sup>(40–42)</sup> The role of income or affordability in fuel choice becomes more evident when all fuels are equally available.<sup>(43,44)</sup> A clear transition has been noted in fuel use, away from firewood and biomass into electricity and LPG, with increasing income.<sup>(45)</sup> Although the observed associations of fuels and ESCC risk may solely be related to SES of individuals using those fuels, the potential effect of emissions from certain cooking fuels on risk of esophageal cancer needs further investigation.

The wealth scores showed an inverse association with ESCC risk. The inverse association between ownership of appliances and ESCC risk may reflect the inverse association between higher economic status and ESCC risk. In addition, ownership of some of the appliances may also be associated with lower risk in some other ways. For example, ownership of a TV may help people to obtain more health-enhancing information compared to those without a TV in their household.

Tobacco use in various forms including cigarettes,<sup>(46–50)</sup> cigars or pipes,<sup>(51)</sup> hookah (water pipe),<sup>(20,52,53)</sup> and bidi,<sup>(54)</sup> as well as chewing in nass and gutka forms,<sup>(52)</sup> has been associated with ESCC. The risk of ESCC associated with tobacco use in high-risk regions of Iran, China, and Kashmir<sup>(5,20,23,52)</sup> is less strong than in Northern America and Central and Eastern Europe,<sup>(55)</sup> which suggests that other factors, including those associated with low SES, may be more important risk factors for ESCC in those areas. Although heavy alcohol use has been associated with an increased ESCC risk,<sup>(11,48,55,56)</sup> drinking of alcohol in Kashmir is infrequent and apparently has little role in the development of ESCC in this region.<sup>(20)</sup>

The strengths of the study are confirmed diagnosis of ESCC, recruitment and interview of subjects by trained staff, and adjustments of results for several potential confounders. This is also the largest study on ESCC carried out in Kashmir. Almost all of the assessed SES indicators in this study were easily recalled factors, including education, house type, and cooking fuel. Limitations of the study include its case-control design, entailing the possibility of selection bias. In addition, although we have adjusted the results for multiple potential confounding factors, the possibility of residual confounding from under adjustments for some of those factors could not be excluded.

In conclusion, this study confirms a strong relationship between low SES and ESCC in Kashmir. These results warrant further studies to understand the possible mechanism lying behind such association.

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## Disclosure statement

The authors have no conflict of interest.

## Abbreviations

B/W TV	black and white television
CI	confidence interval
ESCC	esophageal squamous cell carcinoma
LPG	liquefied petroleum gas
MCA	multiple correspondence analysis
OR	odds ratio
SES	socioeconomic status
SKIMS	Sher-i-Kashmir Institute of Medical Sciences

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