Association between socioeconomic status and mucosal healing in Japanese patients with ulcerative colitis: a cross-sectional study

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ABSTRACT

Objective Socioeconomic status is a risk factor for worse outcomes in many diseases. However, evidence on the association between socioeconomic status and clinical outcome in patients with ulcerative colitis (UC) is limited. In the clinical setting, the therapeutic goal for UC is to achieve mucosal healing (MH). Thus, the aim of this study is to examine the association between socioeconomic status and MH in patients with UC.

Methods The study population consisted of 298 patients with UC. Education status and household income were divided into three groups based on a self-administered questionnaire. MH and complete MH were defined as a Mayo endoscopic subscore of 0–1 and 0, respectively. The association of socioeconomic status with MH and complete MH was assessed by multivariate logistic regression analysis. Patients with UC were divided into a younger group (<51 years old) and an older group (≥51 years old) based on median age.

Results The percentage of MH and complete MH was 62.4% and 25.2%, respectively. In all patients, socioeconomic status was not associated with MH and complete MH, respectively. In the older group, education but not household income was independently positively associated with MH and complete MH. In contrast, in the younger group, no association between socioeconomic status and MH and complete MH was found.

Conclusion In older Japanese patients with UC, education status but not household income was independently positively associated with MH and complete MH.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Several studies of patients with Crohn's disease had revealed an association between socioeconomic status and poor clinical outcomes.
⇒ Evidence regarding this issue in patients with ulcerative colitis (UC) is limited.
⇒ Additionally, the association regarding this issue in patients with UC is inconsistent.
⇒ No study has investigated this issue in Asian patients with UC.

WHAT THIS STUDY ADDS

⇒ Higher education was independently positively associated with mucosal healing and complete mucosal healing in older but not younger patients with UC.
⇒ In contrast, no association between household income and clinical outcome was found, regardless of age.
⇒ This is the first study to show a positive association between education status and clinical outcomes in Asian patients with UC.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Even Asian patients with UC, high education might be protective factor for poor prognosis in patients with UC.
⇒ In older and less educated patients with UC, endoscopies should be performed more frequently, the dose of drug administered should be started higher, and the dose reduction should be slow.

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) that usually requires long-term, lifelong treatment. The estimated prevalence of UC is increasing in Asian countries and remains high in Western countries.[1] Repeated relapses of UC cause poor quality of life, surgery and the risk of colorectal cancer.[2] Both cohort studies and randomised controlled trial showed that mucosal healing (MH) is associated with better outcomes.[2 3]

Maintaining MH is associated with a reduced risk of relapse, fewer surgeries, fewer hospitalisation and steroid tapering. Thus, MH is recommended as the therapeutic goal in clinical setting.[2 3] IBD imposes considerable costs on individuals by affecting their daily lives and social environment. Therefore, socioeconomic status is considered an important

Table 1 Clinical characteristics of 298 study participants

Variable	n (%)
Age, years, mean±SD	50.8±15.9
Men (%)	174 (58.4)
Disease extent (pancolitis/left-sided/proctitis/others)	125/80/86/7
Duration of UC, year, mean±SD	8.6±8.7
BMI, kg/m^2, mean±SD	22.81±4.71
Current smoking (%)	25 (8.4)
Current alcohol intake (%)	123 (41.3)
Medication	
5-Aminosalicylates (%)	248 (90.8)
Prednisolone (%)	62 (20.8)
Thiopurines (%)	444 (14.8)
TNF-α monoclonal antibody (%)	18 (6.0)
Mayo endoscopic subscore, mean±SD	1.20±0.91
Mucosal healing (Mayo endoscopic subscore 0 and 1) (%)	186 (62.4)
Complete mucosal healing (Mayo endoscopic subscore 0) (%)	75 (25.2)
Education, years	
Low (≤12 years) (%)	149 (50.0)
Moderate (12–16 years) (%)	63 (21.1)
High (≥16 years) (%)	86 (28.9)
Household income, Japanese yen/year	
Low (≤2 999 999) (%)	63 (21.1)
Moderate (3 000 000–5 999 999) (%)	139 (46.6)
High (≥6 000 000) (%)	96 (32.2)

Others: right-sided, segmental colitis and postoperative patients (lack of any preoperative medical records of postoperative patients).
BMI, body mass index; TNF, tumour necrosis factor; UC, ulcerative colitis.

factor. Lower socioeconomic status (LSS) might worsen clinical outcomes in many diseases.[4]

Evidence regarding the association between socioeconomic status and clinical outcomes in patients with IBD exists. Most studies of patients with Crohn's disease (CD) showed that education, income and deprivation were associated with poor outcomes.[5] In a Canadian,[6] a French,[7] a British,[8] two Scottish[9 10] and three UC studies of patients with CD,[11–13] socioeconomic status was associated with poor clinical outcomes. In contrast, in patients with UC, evidence regarding the association between socioeconomic status and clinical outcomes is limited and inconsistent. Poor socioeconomic status was associated with mortality in a Canadian study.[14] No association between socioeconomic status and clinical outcomes was found in a British cohort.[5] In contrast, in a Swedish retrospective study of patients with UC, restorative surgery was more common in patients with high income.[15] The association

between socioeconomic status and clinical outcomes in patients with UC remains inconsistent. Additionally, no study has investigated this issue in Asian patients with UC.

In Japan, education status differs for individuals over 50 years of age due to the influence of economic growth.[16] We hypothesised that education status would affect clinical outcomes in patients with UC and that the association between education and clinical outcomes differs between older and younger patients. In the clinical setting, the therapeutic goal for UC is to achieve MH.[2 3 17 18] The purpose of this study was to investigate the association between socioeconomic status and MH in Japanese patients with UC.

METHODS
Study design
This was a cross-sectional study using baseline data from a prospective cohort study.

Study population
The subjects were 387 patients with UC who visited the Department of Gastroenterology and Metabology at the Ehime University Graduate School of Medicine or several affiliated hospitals in Ehime Prefecture, Japan, as inpatients or outpatients between 2015 and 2019. All patients consented to this study and were able to answer the self-administered questionnaire. Subjects were diagnosed with UC based on endoscopic findings and met clinical, radiological and histological criteria. The protocol for this study was developed in accordance with the 1964 Declaration of Helsinki and subsequent versions of the ethical guidelines. Well-trained staff obtained written informed consent from all registered patients.

Measurements
A self-administered questionnaire elicited information regarding smoking, drinking, education and household income. Information on medication for UC, disease extent and duration of UC was obtained from patient medical records. Current smoking was deemed positive if patients answered that they were currently smoking, regardless of the number of cigarettes. Current alcohol intake was deemed positive if patients answered that they had a drinking habit, regardless of the frequency of drinking or the amount of alcohol.

Definition of MH and complete MH
In this study, MH and complete MH were defined as Mayo endoscopic score (MES) category 0–1 and 0, respectively.[19] A certified endoscopist evaluated endoscopic activity by total colonoscopy and reported endoscopic findings and key images. Endoscopist regularly participated in meeting to review endoscopic findings. A single endoscope specialist was responsible for evaluating MES, MH and complete MH at almost the same time as this survey and was blinded to other findings including socioeconomic status.

Table 2 Crude and adjusted ORs and 95% CIs for education status and household income relation to mucosal healing

Variable	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
MH (MES 0–1)			
Education, years			
Low (≤12 years)	90/149 (60.4)	1.00	1.00
Moderate (12–16 years)	40/63 (63.5)	1.14 (0.62 to 2.12)	1.31 (0.66 to 2.67)
High (≥16 years)	56/86 (65.1)	1.22 (0.71 to 2.14)	1.43 (0.77 to 2.69)
P for trend			0.28
Household income, Japanese yen/year			
Low (≤2 999 999)	38/63 (60.3)	1.00	1.00
Moderate (3 000 000–5 999 999)	89/139 (64.0)	1.17 (0.63 to 2.16)	1.39 (0.70 to 2.74)
High (≥6 000 000)	59/96 (61.5)	1.05 (0.55 to 2.09)	1.31 (0.61 to 2.80)
P for trend			0.54
Complete MH (MES 0)			
Education, years			
Low (≤12 years)	35/149 (23.5)	1.00	1.00
Moderate (12–16 years)	16/63 (25.4)	1.11 (0.55 to 2.17)	1.63 (0.74 to 3.55)
High (≥16 years)	24/86 (27.9)	1.26 (0.68 to 2.30)	1.67 (0.86 to 3.27)
P for trend			0.14
Household income, Japanese yen/year			
Low (≤2 999 999)	20/63 (31.8)	1.00	1.00
Moderate (3 000 000–5 999 999)	38/139 (27.3)	0.81 (0.43 to 1.56)	0.86 (0.42 to 1.76)
High (≥6 000 000)	17/96 (17.7)	0.46 (0.22 to 0.97)	0.47 (0.20 to 1.09)
P for trend			0.07

Adjusted for age, sex, use of prednisolone, current alcohol intake, current smoking, BMI, duration of disease, disease extent (pancolitis/non-pancolitis), education and household income.
BMI, body mass index; MES, Mayo endoscopic subscore; MH, mucosal healing.

Statistical analysis

Education status was classified into three categories: (1) low education (junior high school and high school), ≤12 years, (2) moderate education (junior college, vocational technical school and 4-year college dropout), 12–16 years and (3) high education: college or graduate school, 16 years or more. Household income was classified into three categories: (1) low income, ≤2 999 999 Japanese yen/year, (2) moderate income, 3 000 000–5 999 999 Japanese yen/year and (3) high income ≥6 000 000 Japanese yen/year. Age was divided into younger (<51 years old) and older (≥51 years old) groups based on the mean age (50.8 years). Estimations of crude ORs and their 95% CIs for MH and clinical remission in relation to education were performed using logistic regression analysis. Multiple logistic regression analyses were used to adjust for potential confounding factors. Age, sex, use of prednisolone, current alcohol intake, current smoking, body mass index (BMI), duration of disease, disease extent (pancolitis/non-pancolitis), education and household income were selected a priori as potential confounding factors. All statistical analyses were performed using SAS software package V.9.4 (SAS Institute, Cary, North Carolina, USA). All probability values for statistical tests were two-tailed, and p<0.05 was considered statistically significant.

RESULTS

The characteristics of this study

Clinical characteristics of this analysis are shown in table 1. Excluding patients with incomplete data, completed questionnaires were analysed for 77% of patients (298/387). The percentage of MH (MES 0–1) and complete MH (MES 0) was 62.4% and 25.2%, respectively. The education period (years) was 50.0% (n=149) for ≤12, 21.1% (n=63) for 12–16 and 28.9% (n=86) for >16 years, respectively. The percentage of low income, moderate income and high income was 21.1%, 46.6% and 32.2%, respectively. Age was not associated with household income level in this study (data not shown). The percentage of proportion of high and moderate educational levels decreases in patients with 61 years or older; the proportions of patient with low and high education levels were 33.7% and 32.5%, respectively, among those under 40 years old; 48.7% and 30.3%, respectively, among those aged 41–50 years; 38.0% and 36.0%, respectively, among

Table 3 Crude and adjusted ORs and 95% CIs for education status and household income relation to mucosal healing in the younger group

Variable	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
<51 years old (n=164)			
MH (MES 0–1)			
Education			
Low (≤12 years)	44/67 (65.7)	1.00	1.00
Moderate (12–16 years)	27/45 (60.0)	0.78 (0.36 to 1.72)	0.98 (0.38 to 2.44)
High (≥16 years)	30/52 (57.7)	0.71 (0.34 to 1.51)	0.79 (0.34 to 1.87)
P for trend			0.54
Household income, Japanese yen/year			
Low (≤2 999 999)	15/24 (62.5)	1.00	1.00
Moderate (3 000 000–5 999 999)	51/78 (65.4)	1.13 (0.43 to 2.90)	1.25 (0.40 to 3.76)
High (≥6 000 000)	35/62 (56.5)	0.78 (0.29 to 2.02)	1.03 (0.32 to 3.19)
P for trend			0.89
Complete MH (MES 0)			
Education			
Low (≤12 years)	15/67 (22.4)	1.00	1.00
Moderate (12–16 years)	10/45 (22.2)	0.99 (0.39 to 2.44)	1.13 (0.40 to 3.11)
High (≥16 years)	11/52 (21.2)	0.93 (0.38 to 2.23)	0.97 (0.37 to 2.45)
P for trend			0.90
Household income, Japanese yen/year			
Low (≤2 999 999)	7/24 (29.2)	1.00	1.00
Moderate (3 000 000–5 999 999)	20/78 (25.6)	0.84 (0.31 to 2.43)	0.82 (0.27 to 2.59)
High (≥6 000 000)	9/62 (14.5)	0.41 (0.13 to 1.31)	0.43 (0.13 to 1.48)
P for trend			0.12

Adjusted for age, sex, use of prednisolone, current alcohol intake, current smoking, BMI, duration of disease, disease extent (pancolitis/non-pancolitis), education and household income.
BMI, body mass index; MES, Mayo endoscopic subscore; MH, mucosal healing.

those aged 51–60 years and 73.0% and 20.2%, respectively, among those aged 61 years or older.

Association between socioeconomic status and endoscopic activity

The association between socioeconomic status and MH in all patients is shown in table 2. Education status was not associated with MH and complete MH. In crude analysis, high income was inversely associated with complete MH (crude OR 0.46, 95% CI 0.22 to 0.97). After adjustment for confounding factors, the association between high income and complete MH disappeared.

Association between socioeconomic status and endoscopic activity after age stratification at time of survey

Crude and adjusted ORs and 95% CIs for socioeconomic status related to MH and complete MH in the younger group (table 3) and the older group (table 4) are shown. No association between socioeconomic status and clinical outcome was found in the younger group. In the older group, higher education was significantly and positively associated with MH (MH: crude OR 2.54, 95% CI 1.06 to 6.62). After adjustment for age, sex, use of prednisolone, current alcohol intake, current smoking, BMI, duration of disease, disease extent, education and household income, higher education was independently positively associated with MH and complete MH, respectively (MH: adjusted OR 3.27, 95% CI 1.14 to 10.48 and complete MH: adjusted OR 3.19, 95% CI 1.13 to 9.44). After excluding patients with UC diagnosis of 1 year or less, the positive association between education status and MH was significant (data not shown). In contrast, no association between household income and clinical outcome was found.

DISCUSSION

In this study, higher education was independently positively associated with MH and complete MH in older but not younger patients with UC. In contrast, no association between household income and clinical outcome was found, regardless of age. This is the first study to show a positive association between education status and clinical outcomes in Asian patients with UC.

Table 4 Crude and adjusted ORs and 95% CIs for education status and household income relation to mucosal healing in the older group

Variable	Prevalence (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
≥51 years old (n=134)			
MH (MES 0–1)			
Low (≤12 years)	46/82 (56.1)	1.00	1.00
Moderate (12–16 years)	13/18 (72.2)	2.04 (0.70 to 6.82)	2.67 (0.76 to 10.64)
High (≥16 years)	26/34 (76.5)	2.54 (1.06 to 6.62)	3.27 (1.14 to 10.48)
P for trend			0.020
Household income, Japanese yen/year			
Low (≤2 999 999)	23/39 (59.0)	1.00	1.00
Moderate (3 000 000–5 999 999)	38/61 (62.3)	1.15 (0.50 to 2.62)	1.20 (0.47 to 3.06)
High (≥6 000 000)	24/34 (70.6)	1.67 (0.64 to 4.53)	1.24 (0.37 to 4.29)
P for trend			0.67
Complete MH (MES 0)			
Education			
Low (≤12 years)	20/82 (24.4)	1.00	1.00
Moderate (12–16 years)	6/18 (33.3)	1.55 (0.49 to 4.56)	3.02 (0.77 to 11.81)
High (≥16 years)	13/34 (38.2)	1.92 (0.81 to 4.52)	3.19 (1.13 to 9.44)
P for trend			0.027
Household income, Japanese yen/year			
Low (≤2 999 999)	13/39 (33.3)	1.00	1.00
Moderate (3 000 000–5 999 999)	18/61 (29.5)	0.84 (0.35 to 2.01)	0.81 (0.30 to 2.23)
High (≥6 000 000)	8/34 (23.5)	0.62 (0.21 to 1.71)	0.41 (0.11 to 1.44
P for trend			0.19

Adjusted for age, sex, use of prednisolone, current alcohol intake, current smoking, BMI, duration of disease, disease extent (pancolitis/non-pancolitis), education and household income.
BMI, body mass index; MES, Mayo endoscopic subscore; MH, mucosal healing.

Evidence of an association between socioeconomic status, including household income status, and clinical outcomes in patients with IBD exists (online supplemental file 1). In a Canadian database study of 9298 patients with IBD, LSS was associated with intensive care unit admission, hospital mortality, surgery and high dose steroid use.[6] In a US study of 323 patients with IBD including 138 patients with UC, low annual income but not high education was positively associated with moderate to severe disability based on IBD Disability Index score.[13]

In most studies of patients with CD, poor socioeconomic status might worsen clinical outcomes. In a French prospective study of 207 patients with CD, deprivation was associated with hospitalisation.[7] In a US retrospective study of 944 patients with CD, low household income was associated with the hospitalisation rate.[11] In a US database study of patients with CD, above-average income was associated with lower in-hospital mortality.[12] In a British study, no association between social deprivation and mortality is found, while the hospitalised prevalence of CD was slightly higher in the most deprived area.[8] In a Scottish study of 1595 inpatients with CD, social deprivation was significantly associated with 3 years mortality.[9]

Another Scottish database study showed that deprivation status was associated with 3-year mortality after hospitalisation.[10]

In contrast, limited evidence regarding socioeconomic status and clinical outcome in patients with UC exists, and their association has been inconsistent. A British study showed that no association between living in socially disadvantaged areas and clinical outcome including hospitalisation and mortality.[8] In a Canadian population-based study of patients with IBD, LSS was associated with mortality in patients with UC.[14] In a Swedish retrospective study of 5969 patients with UC, no association between socioeconomic status and the risk of failure after restorative surgery was found, while restorative surgery was more common in patients with high income but not education level.[15] The discrepancies between the findings in this study and those of previous studies can be partly explained by age, education status, income status, definition of clinical outcome and medical systems.

The mechanisms underlying the association between education status and clinical outcome remain unclear. LSS affects medication adherence[20] and access to healthcare.[21] In a Japanese study of patients with chronic

disease, advanced education is associated with good adherence.[22] Similarly, in patients with diabetes, adherence is associated with high education.[23] However, Indian study of patients with IBD, poor adherence was observed in patients with professional or honours and middle school certificate/primary school, while good adherence is found in patients with intermediate or post high school diploma/high school certificate, graduate or postgraduate and illiterate.[24] In a French mail-based studies of patients, education is not associated with adherence.[25] The association between education status and adherence is inconsistent. In an Indian study, the first reason for non-adherence was reported as forgetting the medication, and the third reason was feeling well. The good clinical course may be making patients less aware of the need for treatment, resulting in lower adherence. A considerable heterogeneity in the adherence rates had been reported in patients with IBD.[26] In Japan, the percentage of advanced education in the young population is higher than that in the older population. Therefore, at younger ages, differences in education may have a disappearing influence on clinical outcomes. In Japan, the medical insurance system provides standard medication for all patients with UC, regardless of household income. Additionally, the public medical expense subsidy for UC might mask the association between household income and clinical outcomes in UC. Advanced education might lead to more MH via more access to examinations and healthcare. The mechanism of why education is preventive is unknown, and research on the identification of unknown factors associated with education is needed.

In several studies of patients with CD, low socioeconomic status is associated with poor clinical outcomes. In the contrast, in studies of patients with UC, the association between socioeconomic status and clinical outcomes is inconsistent. Socioeconomic status might affect the clinical outcomes in CD more than those in UC.[5] However, few studies on this topic were conducted in studies of patients with UC. In Japan, the universal health insurance system and subsidies for UC treatment have greatly reduced the high cost of UC treatment, and hospitalisation and surgery have little impact on income. Japan's universal health insurance system and social security might weaken the influence of socioeconomic status to clinical outcomes. Additionally, social health insurance differs from country to country, further more studies regarding this issue in patients with UC is needed.

This study has some limitations. First, the cross-sectional study design failed to demonstrate a causal relationship between education status and UC disease activity. Second, this study used a self-administered questionnaire. Although there are no data on the validity of self-reports of education status and household income, any possible misclassification of non-discriminatory exposure would introduce a bias toward the null hypothesis. We could not assess the reduction of household income due to hospitalisation and/or intensified treatment. Low socioeconomic status may worse disease activity.

Hospitalisation and absence from work might worse the socioeconomic status. However, in Japan, the universal health insurance system and subsidies for UC treatment have greatly reduced the high cost of UC treatment, and hospitalisation and surgery have little impact on income. Japan's universal health insurance system and social security might mask the true association between household income and clinical outcomes. Third, although employment status is strongly associated with socioeconomic status, data regarding patient employment status is lacking. Fourth, education, income and medical systems different among countries. Thus, generalisation of the findings of this study might be difficult for other ethnic populations. Fifth, we did not used central reading of endoscopic findings in the study. Sixth, we could not assess other clinical outcomes including hospitalisation, operation and morality due to sample size. Finally, selection bias may have influenced the results of this study. The percentage of biologics use might be low in this cohort. This study was probably not representative of all Japanese patients with UC. However, In Japan, medical checkups are widely conducted to screen for colorectal cancer screening using faecal occult blood test. Endoscopic examination is performed for subjects with faecal occult blood test positive, regardless of symptoms. The cohort may include patients with UC with no symptoms but only positive faecal occult blood. Japanese medical checkups might detect no symptomatic patients with UC and lower the percentage of biologics use in the cohort. However, the mean age, sex ratio and drug dosage in this study were similar to those in Japanese national surveys on UC.[27]

In conclusion, education status but not household income was independently positively associated with MH and complete MH in older Japanese patients with UC. In younger Japanese patients with UC, socioeconomic status might not be associated with clinical outcome. In older and less educated patients with UC, endoscopies should be performed more frequently, the dose of drug administered should be started higher, and the dose reduction should be slow.

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Supplemental material

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1   Supplement file. Socioeconomic status and clinical outcomes in patients with IBD

Nation	Years	Subjects, number	Socioeconomic status	Clinical outcomes
Canada[6]	2020	IBD, 9,298	LSS	Physician visits, hospitalization, intensive care unit administration, use of steroid, and death
France[7]	2009	CD, 207	Deprivation	Hospitalization, and surgery
UK[8]	2010	CD, 1,467 UC, 1482	Deprivation area	CD, hospitalization UC, no association
Scottland[9]	2011	Inpatient CD, 1,595	Social Deprivation	3-years mortality
Scottland[10]	2014	CD	Deprivation	Mortality
US[11]	2018	CD, 944	Low income, and below poverty level	Hospitalization
US[12]	2007	Inpatient CD, 41,918	Insurance status, residence area (above median income)	Insurance, low surgery Area, low in-hospital mortality
US[13]	2019	CD, 185 UC, 138	Household income	Moderate to severe disability
Canada[14]	2015	CD and UC, 10,788	LSS	Mortality
Sweden[15]	2021	UC patients with colectomy, 5,969	High income and education	Income, high rete restorative surgery (No association, fail of surgery) Education, no association

2   LSS, lower socioeconomic status; CD, Crohn's disease; UC, ulcerative colitis