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Age of onset, sociodemographic, and clinical predictors of depression: a population-based study in Rural Southern Iran

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Abstract

Background Depression is the leading cause of disability worldwide and a growing public health concern. In Iran, the prevalence of depression has shown an increasing trend, with rural populations facing unique challenges in access to mental health care. This study aimed to determine sociodemographic and clinical predictors of depression and explore how these factors influence age at onset in a rural population, providing valuable insights for preventive strategies.

Methods The present cross-sectional investigation utilized baseline data of the Fasa PERSIAN Cohort, comprising 10,133 adults aged 35 and older from a rural region in southern Iran. Depression diagnoses were based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. Logistic regression analyses were conducted to identify predictors of depression, while linear regression models examined associations between baseline characteristics and age at depression onset.

Results Among participants, 6.7% met the criteria for depression, with a higher prevalence among females (78.7%) and the unemployed (70.9%). Independent predictors included female sex, unemployed status, literacy, diabetes, fatty liver disease, and psychiatric comorbidities, which emerged as the strongest predictor (odds ratio = 6.605, $p < 0.001$). The average age at depression onset was 39.5 years, with men experiencing onset earlier than women. Earlier onset was also associated with higher education levels, opioid use, psychiatric comorbidities, and higher energy intake, whereas later onset was linked to medical conditions, including hypertension, cardiovascular disease, and stroke.

Conclusion This study highlights important demographic and clinical factors linked to depression and its age of onset, underscoring the complex interplay between sociodemographic characteristics, lifestyle factors, and comorbidities. These findings can guide targeted mental health interventions and support tailored prevention strategies in similar rural populations.

Keywords Depression, Age of onset, Sociodemographic factors, Clinical factors, Rural population

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Introduction

Depression, a major global public health concern, is both a leading cause of disability worldwide and a key risk factor for numerous medical complications, especially among aging populations [1]. A few years ago, in 2015, depression was considered the third most significant cause of global disability [2]. However, the significant burden of depression has not only continued but has also grown over recent years, making it the most common psychiatric disorder currently and the primary cause of disability in adults [3]. In Iran, depression is ranked as the third most important health-related problem and imposes considerable pressure on individuals and society as well as the health provider systems [4].

Depression appears prevalent across both urban and rural populations. However, residents in rural areas represent a particularly vulnerable group, characterized by higher poverty rates, limited access to health insurance, poorer overall health status, and greater prevalence of chronic health conditions [5]. Furthermore, rural regions typically experience inadequate availability of social services, healthcare resources, and especially mental health support, with existing services often described as fragmented and inconsistent [6, 7]. These factors may contribute to differences in the prevalence of depression and its associated determinants between rural and urban populations.

Although extensive research has identified numerous sociodemographic and environmental risk factors for depression, there are remarkable disparities. In this context, a large-scale meta-analysis revealed that people with a low socioeconomic level, characterized by limited educational level, low income, unsatisfactory occupational roles, lower social class, or fewer assets, have an almost 1.8-fold higher chance of presenting depression compared to individuals with a more favorable socioeconomic status [8]. Furthermore, the Global Burden of Disease Study indicates that major depression occurs more frequently in females compared to males (5·5% of women versus 3·2% of men) [9]. Other key risk factors include low education levels [10], relationship dissolution [11], and financial instability [12]. These sociodemographic factors emphasize the need for a comprehensive and inclusive strategy to identify vulnerable populations and improve mental health outcomes across diverse groups.

In addition to social and demographical indicators, certain medical and psychological conditions serve as critical risk factors for depression. Physical illnesses, including diabetes, coronary heart disease (CHD), and chronic obstructive pulmonary disease, are consistently linked to elevated depression rates because of their adverse effects on daily functioning and quality of life [13, 14]. Furthermore, other mental health conditions, particularly anxiety and post-traumatic stress disorder (PTSD), frequently co-occur with depression, often exacerbating its severity and persistence [15]. Together, these clinical factors underscore the intricate interaction between physical and mental health in contributing to depressive outcomes [16].

Age at onset is another critical dimension of depression, as it influences disease progression and outcomes. Depression typically begins around age 30 [17], but earlier onset is associated with more severe complications, including a heightened risk of co-occurring other mental health disorders and an increased likelihood of suicide [18, 19]. In contrast, late-onset depression, particularly in older individuals, is correlated with prolonged hospitalizations and specific physical health complications [20]. Studies have also identified factors influencing age at onset, with early onset linked to low socioeconomic status and family history [21], while adequate physical activity in older adults appears to delay depressive symptoms [22]. Understanding the predictors of age at onset is essential for improving prevention and intervention strategies.

Although the body of research on depression predictors is expanding, there has been limited focus on rural populations and the factors influencing the age of onset. Addressing this gap, the current study aimed to explore the clinical and sociodemographic predictors of depression within a large rural population in southern Iran. Additionally, it sought to investigate the relationship between these factors and the age of depression onset, providing valuable insights into an often-overlooked dimension of mental health.

Material and methods

Study design and population

This cross-sectional study analyzed baseline data from over 10,000 individuals enrolled in the Fasa PERSIAN Cohort study [23–25]. This cohort is one of 22 ongoing cohort studies in Iran and was conducted among residents of Sheshdeh, a rural area located approximately 40 km from Fasa city in southern Iran. The sampling method used in this study was a census approach. Initially, one suburban region (Sheshdeh) was randomly selected from three suburbs surrounding the city of Fasa. Subsequently, all eligible individuals within this selected area were invited to participate, based on comprehensive population records obtained from local health authorities and community health workers (Behvarz). Since we invited the entire eligible population rather than employing stratified or simple random sampling, the participants included are expected to be highly representative of the community residing in the selected region.

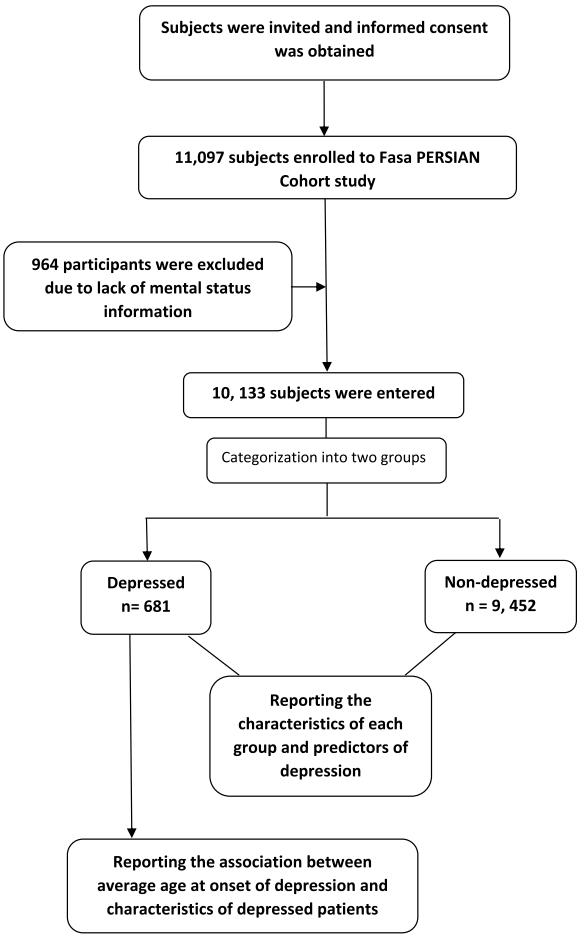

Fig. 1 Flowchart of participant selection and study method

Data collection began in November 2014 and continued until June 2019, ultimately including 11,097 individuals aged 35 or above who had resided in Sheshdeh for at least nine months per year. The primary aim of the cohort was to identify predisposing factors for non-communicable diseases among participants, over a planned follow-up period of 15 years. Before enrollment, written informed consent was obtained from all participants or their legal guardians if they were illiterate. Participants also retained the right to withdraw at any time during the study. After excluding 964 (8.68%) individuals due to missing mental health data, a total of 10,133 participants were included into our study. We summarized the study method in Fig. 1.

Depression assessment

In this study, depression among participants was diagnosed by an attending psychiatrist using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for major depressive disorder [26]. To address the secondary objective, the age of depression onset was determined as the age at which participants received their initial diagnosis of depression from an attending psychiatrist, based on the same DSM-IV standards. Participants in Sheshdeh benefit from comprehensive, free-of-charge healthcare coverage under Iran's Family Medicine Program. Through routine care, family physicians identify early symptoms of depression and promptly refer patients to psychiatric specialists available in the region two days per week. However, potential barriers such as cultural stigma, socioeconomic factors, and individual reluctance may occasionally delay individuals from seeking specialized mental healthcare. Thus, the reported age of depression onset in this study should be regarded as an approximation rather than the precise age at symptom initiation.

Measurements

The study population completed two questionnaires: one gathering general demographic information-such as sex, age, educational background, and occupational status-and the other collecting clinical and lifestyle data, including chronic disease history, medication use, and consumption of alcohol, opium, and tobacco (encompassing both active and passive smoking exposure). Sex was defined as male or female based on the designation assigned at birth. Education was categorized into five levels: illiterate, primary education, middle school, high school diploma, and post-diploma or higher education. Information on smoking, alcohol consumption, and opium use was collected based on participants' self-reports, specifically by asking whether they had smoked or used alcohol or opium within the past 12 months.

Chronic diseases, including diabetes, hypertension, cardiovascular disease (CVD), fatty liver disease (FLD), chronic lung disease, stroke, rheumatoid disease, and other psychiatric disorders, were recorded as part of each participant's medical history. In this study, "other psychiatric disorders" refer to any diagnosed mental health conditions reported by participants, aside from depressive disorder. These include anxiety disorders (such as generalized anxiety disorder, panic disorder, and social anxiety disorder), bipolar disorders (bipolar I and II), schizophrenia spectrum and other psychotic disorders (including schizophrenia and schizoaffective disorder), personality disorders (e.g., borderline, antisocial, narcissistic), substance use disorders (e.g., alcohol, opioid, stimulant use disorders), PTSD, obsessive–compulsive disorder (OCD), and eating disorders (such as anorexia nervosa and bulimia nervosa). Body mass index (BMI) was determined by dividing an individual's weight in kilograms by the square of their height in meters.

Physical activity was assessed using a 20-item questionnaire specifically designed to capture common activities among the Iranian rural population. The metabolic equivalent score (MET) was calculated based on the International Physical Activity Questionnaire (IPAQ), which was used to quantify physical activity. For each activity, the daily duration (in hours) was multiplied by its corresponding MET value, and total physical activity was expressed as MET-hours per day [27]. Energy intake (EI) was estimated using Nutritionist IV software (version 7.0) after participants completed a modified 125-item food frequency questionnaire (FFQ), as referenced by [23]. The full set of data collection forms and questionnaires can be accessed through the website ncdrc.fums.ac.ir.

Statistical analysis

Quantitative variables were presented as mean ± standard deviation (SD), while qualitative variables were reported as frequencies (number and percentage). Independent samples t-tests were used to compare two groups, and one-way ANOVA with post hoc LSD tests was applied for comparisons among three or more groups. Correlation coefficients were used for relationships between quantitative variables, while the chi-square test was employed for categorical variables. Logistic regression models were employed to evaluate the association between the independent variables and depression among all participants, with results presented as significance levels, odds ratios (OR), and 95% confidence intervals (CI). Additionally, a linear regression model was applied to investigate the relationship between the average age at depression onset and baseline characteristics among depressed patients. The results are reported as standardized beta coefficients (B) with their corresponding *p*-values. Model assumptions, including normality, linearity, and homoscedasticity, were assessed and met. In both models, variables with a *p*-value below 0.2 in the univariate analysis were considered potential predictors for inclusion in multivariate analysis. All statistical analyses were performed using IBM SPSS Statistics v27, with significance defined as a *p*-value less than 0.05 and a 95% CI.

Ethics statement

The study protocol adhered to the principles outlined in the Helsinki Declaration. In addition, this project was initiated after receiving authorization from the Ethics Committee of Fasa University of Medical Sciences on May 18, 2022, with approval code IR.FUMS.REC.1401.010. The study maintains the confidentiality of participants' identities and sensitive information.

Results

Cohort profile and the association between demographic and clinical characteristics with depression

A total of 10,133 participants were enrolled in the study, comprising 4,575 males (45.1%) and 5558 (54.9%) females. Table 1 presents the baseline characteristics of all subjects, categorized by their depression status. Overall, a small portion of the cohort ($n=681$, 6.72%) met the DSM-IV criteria for depression. Among depressed subjects, the majority were female ($n=536$, 78.7%), compared to just over half ($n=5,022$, 53.1%) in the non-depressed group, reflecting a statistically significant sex disparity ($p<0.001$). While the number of employed and unemployed people was similar in the non-depressed group, depressed cases exhibited a significantly higher unemployment rate ($p<0.001$). Moreover, education levels differed significantly between depressed and non-depressed individuals ($p=0.001$).

Notably, smoking status (active or passive) and opium use were more prevalent among non-depressed participants than among those with depression, with statistically significant associations ($p<0.001$). Analysis of medical comorbidities showed that diabetes, hypertension, CVD, FLD, chronic lung disease, stroke, and rheumatoid disease were all more common among depressed individuals compared to healthy ones. Also, a higher prevalence of other psychiatric disorders was observed among depressed participants. All these associations were significant ($p<0.05$).

Non-depressed participants also had a higher average EI ($p<0.001$) and engaged in more weekly physical activity (measured in METs, $p<0.001$) compared to depressed subjects. Conversely, BMI was notably greater in the depressed group than in the non-depressed group ($p<0.001$). Detailed information on the associations between these variables and depression status are provided in Table 1.

Variables demonstrating a significant association with depression were incorporated into the logistic regression analysis. As presented in Additional file 1, the analysis identified several independent predictors of depression: female sex ($p<0.001$, OR = 3.062), employment status ($p=0.017$, OR = 0.743), primary education ($p<0.001$, OR = 1.745), middle school education ($p<0.001$, OR = 2.012), high school diploma ($p=0.004$, OR = 1.828), university education ($p=0.049$, OR = 1.888), diabetes ($p=0.046$, OR = 1.262), fatty liver disease ($p=0.012$, OR = 1.347), and other psychiatric disorders ($p<0.001$, OR = 6.605). Notably, individuals with psychiatric comorbidities exhibited the highest odds of depression. Other variables, however, were not independently associated with depression risk in the adjusted model (see Fig. 2).

Table 1 Baseline characteristics of the 10133 non-depressed and depressed subjects

Variables	Total (*N* = *10,133*)	Depressed (*N* = *681*)	Non-Depressed (*N* = *9452*)	*P*-value
Sex				< 0.001*
Male	4575 (45.1%)	145 (21.3%)	4430 (46.9%)	
Female	5558 (54.9%)	536 (78.7%)	5022 (53.1%)	
Occupation status				< 0.001*
Employed	5091 (50.3%)	198 (29.1%)	4893 (51.9%)	
Unemployed	5022 (49.6%)	482 (70.9%)	4540 (48.1%)	
Level of education				0.001*
Illiterate	4646 (45.8%)	275 (40.4%)	4368 (46.3%)	
Primary education	3292 (32.5%)	267 (39.2%)	3024 (32.0%)	
Middle school education	1358 (13.4%)	95 (14.0%)	1263 (13.4%)	
Diploma	604 (6.0%)	32 (4.7%)	571 (6.0%)	
Post-diploma or higher	234 (2.3%)	12 (2.3%)	222 (2.3%)	
Sociodemographic status				0.913
Poor	3366 (33.2%)	222 (32.6%)	3144 (33.3%)	
Intermediate	3316 (32.7%)	222 (32.6%)	3094 (32.8%)	
High	3444 (34.0%)	236 (34.7%)	3208 (34.0%)	
Active smoker				< 0.001*
Yes	2738 (27.0%)	127 (18.6%)	2611 (27.6%)	
No	7395 (73.0%)	554 (81.4%)	6841 (72.4%)	
Passive smoker				< 0.001*
Yes	1886 (18.6%)	90 (13.2%)	1796 (19.0%)	
No	8247 (81.4%)	591 (86.8%)	7656 (81.0%)	
Alcohol consuming				0.061
Yes	485 (4.8%)	22 (3.2%)	463 (4.9%)	
No	9648 (95.2%)	659 (96.8%)	8989 (95.1%)	
Opioid use				< 0.001*
Yes	2113 (20.9%)	86 (12.6%)	2027 (21.4%)	
No	8020 (79.1%)	595 (87.4%)	7425 (78.6%)	
Diabetes				< 0.001*
Yes	1249 (12.3%)	127 (18.6%)	1122 (11.9%)	
No	8883 (87.7%)	554 (81.4%)	8329 (88.1%)	
Hypertension				< 0.001*
Yes	2030 (20.0%)	192 (28.2%)	1838 (19.4%)	
No	8102 (80.0%)	489 (71.8%)	7613 (80.6%)	
Cardiovascular disease				< 0.001*
Yes	1099 (10.8%)	111 (16.3%)	988 (10.5%)	
No	9033 (89.2%)	570 (83.7%)	8463 (89.5%)	
Stroke				0.016*
Yes	124 (1.2%)	15 (2.2%)	109 (1.2%)	
No	10,009 (98.8%)	666 (97.8%)	9343 (98.8%)	
Fatty liver disease				< 0.001*
Yes	1048 (10.3%)	135 (19.8%)	913 (9.7%)	
No	9084 (89.7%)	546 (80.2%)	8538 (90.3%)	
Chronic lung disease				< 0.001*
Yes	187 (1.8%)	26 (3.8%)	161 (1.7%)	
No	9945 (98.2%)	655 (96.2%)	9290 (98.3%)	
Rheumatic disease				< 0.001*
Yes	503 (5.0%)	57 (8.4%)	446 (4.7%)	
No	9629 (95.0%)	624 (91.6%)	9005 (95.3%)	

Table 1 (continued)

Variables	Total (*N* = *10,133*)	Depressed (*N* = *681*)	Non-Depressed (*N* = *9452*)	*P*-value
Other psychiatric disorders				< 0.001*
Yes	915 (9.0%)	256 (37.6%)	659 (7.0%)	
No	9218 (91.0%)	425 (62.4%)	8793 (93.0%)	
EI (kcal/day)	2936.01 ± 1143.70	2651.43 ± 985.69	2956.66 ± 1151.72	< 0.001*
Physical activity (Met-h/day)	41.49 ± 11.28	38.86 ± 8.74	41.63 ± 11.50	< 0.001*
BMI (Kg/m^2)	25.65 ± 4.82	26.66 ± 4.80	25.57 ± 4.85	< 0.001*

Data are reported as mean ± standard deviation or as numbers (percentages). Student t-test were used for age, EI, MET, and BMI, remaining categorical outcomes were compared by Pearson's Chi-square, *P*-value < 0.05 is considered significant. *EI* Energy intake, *BMI* Body mass index, *MET* Metabolic equivalent, * indicates significance

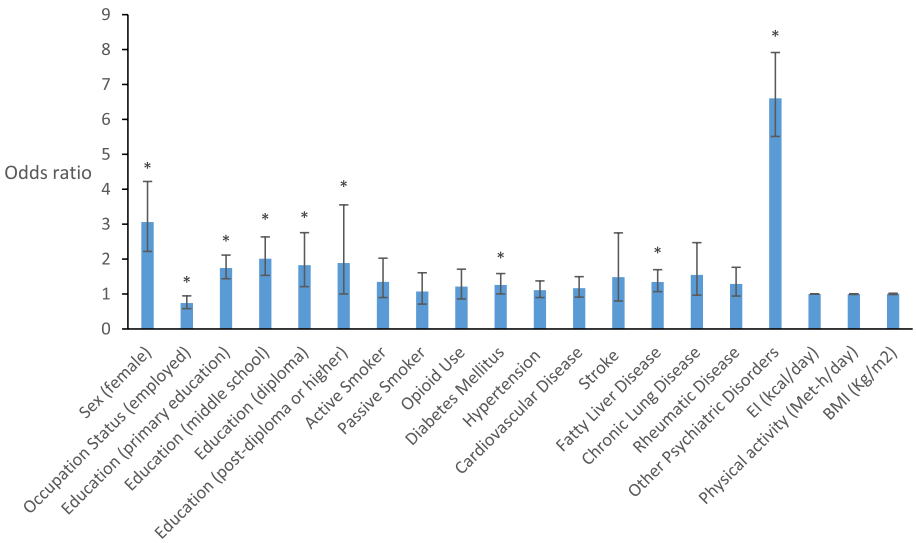

Fig. 2 OR and 95%CI of the depression predictors based on the multivariate adjusted logistic regression analysis. *Indicates statistically significant odds ratios (*p*-value < 0.05)

Correlation between average age at onset of depression with demographic and clinical profiles of depressed individuals

Among the 681 participants diagnosed with depression, the average age at the first confirmed diagnosis (based on DSM-IV criteria) was 39.48 ± 10.51 years. Table 2 demonstrates the association between the onset age of depression and various qualitative and quantitative variables. Depression was diagnosed approximately 2.5 years earlier in males compared to females ($p = 0.017$). In addition, the mean age of onset differed significantly between employed and unemployed individuals (37.49 ± 9.41 versus 40.27 ± 10.84 years, $p = 0.001$). A significant variation in age of onset was also observed across the five education levels ($p < 0.001$).

Passive smokers were diagnosed with depression at a later age compared to those with no exposure to smoking ($p = 0.031$). In contrast, alcohol and opium consumption were significantly associated with a younger age of depression onset ($p = 0.044$ and $P = 0.017$, respectively). Regarding clinical characteristics, individuals with diabetes, hypertension, CVD, or a history of stroke experienced a later average onset of depression than their healthier counterparts in each respective group, with all associations reaching statistical significance ($p < 0.05$). Conversely, the presence of other psychiatric comorbidities was linked to an earlier onset of depression ($p = 0.001$). Lastly, energy intake showed a significant negative correlation with the age at depression onset ($p = 0.005$).

After multivariate adjustment in the linear regression analysis, higher educational attainment, opium use, the presence of other psychiatric comorbidities, and higher EI were significantly correlated with a younger age at onset of depression. Conversely, passive smoking as well as hypertension, CVD, and stroke, showed significant associations with an older age at onset of depression. Among the predictors, stroke demonstrated

Table 2 Average age at onset of depression stratified by target variables among depressed subjects ($n=681$)

Variables	Average age at onset of depression (mean ± SD)	*P*-value
Sex		0.017*
Male	37.57 ± 10.88	
Female	39.99 ± 10.36	
Occupation status		0.001*
Employed	37.49 ± 9.41	
Unemployed	40.27 ± 10.84	
Level of education		< 0.001*
Illiterate	44.34 ± 11.19	
Primary education	37.54 ± 8.72	
Middle school education	33.83 ± 8.05	
Diploma	32.53 ± 6.38	
Post-diploma or higher	34.25 ± 8.87	
Active smoker		0.454
Yes	40.11 ± 11.80	
No	39.33 ± 10.21	
Passive smoker		0.031*
Yes	41.70 ± 11.74	
No	39.14 ± 10.28	
Alcohol consuming		0.044*
Yes	35.05 ± 9.35	
No	39.63 ± 10.52	
Opioid use		0.017*
Yes	36.95 ± 9.87	
No	39.84 ± 10.56	
Diabetes		0.006*
Yes	41.94 ± 11.25	
No	38.91 ± 10.27	
Hypertension		< 0.001*
Yes	44.09 ± 11.03	
No	37.66 ± 9.73	
Cardiovascular disease		< 0.001*
Yes	44.41 ± 12.29	
No	38.52 ± 9.86	
Fatty liver disease		0.625
Yes	39.87 ± 11.02	
No	39.38 ± 10.39	
Chronic lung disease		0.755
Yes	38.85 ± 11.16	
No	39.50 ± 10.49	
Stroke		0.002*
Yes	47.80 ± 11.60	
No	39.29 ± 10.42	
Rheumatoid disease		0.189
Yes	41.23 ± 11.30	
No	39.32 ± 10.43	
Other psychiatric disorders		0.001*
Yes	37.82 ± 10.34	
No	40.48 ± 10.50	
EI (kcal/day) (r)	- 0.108	0.005*
BMI (Kg/m^2) (r)	- 0.036	0.345
Physical activity (Met-h/day) (r)	- 0.039	0.312

Analysis of variance (ANOVA) used for marital status and level of education, Pearson correlation coefficient (*r*) used for MBI, physical activity, and EI, remaining variables were compared by Student t-test, *P*-value < 0.05 is considered significant. *SD* standard deviation, *EI* energy intake, *BMI* body mass index, *MET* metabolic equivalent, * Indicates significance

the strongest positive association with age at onset (B = 6.969, $p=0.032$), while the presence of other psychiatric disorders had the strongest negative association (B = -5.639, $p<0.001$). The beta coefficients and *p*-values for both unadjusted and adjusted regression models are summarized in Table 3.

Discussion

Despite significant efforts to reduce the impact of depression, it remains a critical global challenge, particularly in low- and middle-income countries [28]. Depression is not only one of the leading causes of disability worldwide [29] but also the primary risk factor for suicidal behaviors [30]. A systematic analysis published in 2019 reported that around 280 million people globally are struggling with depression [31]. In our study population, the prevalence of depression was also noteworthy, with 681 cases out of 10,133 (6.7%). This figure falls within the range of reported national estimates. A systematic review of 44 studies using diagnostic interviews reported a pooled current prevalence of 4.1% in the general population [32], while the 2011 IranMHS national survey estimated a 12-month prevalence of 12.7% among adults aged 15–64 years [33]. More recent estimates suggest that one in eight adults in Iran suffers from major depressive disorder (MDD), highlighting a rising trend [34]. Alarmingly, this rate is expected to increase further by 2030 [35]. This variation in reported prevalence across national studies may be attributed to differences in diagnostic methods, study populations, and the time periods in which the studies were conducted. Consequently, this research aimed to identify clinical and sociodemographic predictors of depression in a large adult population and to investigate the association between these factors and the age of depression onset.

Predictors of depression

Firstly, our analysis revealed a pronounced sex disparity, with females experiencing depression nearly three times more often than males [36]. This finding aligns

Table 3 Linear regression analysis examining associations between variables and average age at depression onset in depressed subjects

Variables	Univariate Regression			Multivariate Regression		
	p-value	B	95% CI	*p*-value	B	95% CI
Sex (female)	0.014*	1.992	0.407, 3.577	0.333	-1.045	-3.166, 1.075
Occupation Status (employed)	0.002*	-2.523	-4.098, -0.948	0.696	-0.371	-2.234, 1.492
Education (higher levels)	< 0.001*	-3.897	-4.624, -3.169	< 0.001*	-3.315	-4.049, -2.580
Passive smoker	0.031*	2.231	0.201, 4.260	< 0.001*	4.356	2.257, 6.455
Alcohol Consuming	0.044*	-3.796	-7.497, -0.095	0.679	-0.737	-4.228, 2.755
Opioid Use	0.017*	-2.363	-4.305, -0.421	0.015*	-2.751	-4.969, -0.533
Diabetes	0.003*	3.585	1.190, 5.980	0.526	0.709	-1.483, 2.900
Hypertension	< 0.001*	7.232	5.329, 9.136	< 0.001*	4.302	2.387, 6.218
Cardiovascular disease	< 0.001*	6.999	4.505, 9.492	0.002*	3.714	1.352, 6.075
Stroke	0.002*	11.369	4.212, 18.525	0.032*	6.969	0.589, 13.349
Other Psychiatric Disorders	0.001*	-4.500	-7.244, -1.757	< 0.001*	-5.639	-8.082, -3.196
EI (kcal/day)	0.005*	-0.001	-0.002, 0.00	0.026*	-0.001	-0.001, 0.00

B Beta coefficient, *CI* Confidence interval, *EI* Energy intake. *Indicates significance

with existing literature, which consistently identifies being female as a significant risk for presenting depression [37]. The greater prevalence of depression among women is probably affected by a combination of factors, including genetic predispositions, hormonal influences, and physiological stress responses, rather than a single specific mechanism [38]. Unemployment also emerged as a notable predictor of depression in our study, mirroring prior research on the psychological toll of job loss [39]. The connection is clear: unemployment undermines self-worth, diminishes financial security, and increases vulnerability to depressive symptoms [40].

Education level presented an intriguing finding. Compared to illiteracy, individuals with higher levels of education showed an increased tendency to experience depression, diverging from earlier studies that highlighted the protective benefits of education against mental health challenges [36, 41]. Although higher education is typically associated with increased income, job security, better access to healthcare, and stronger social support networks [42], our findings suggest otherwise. Factors contributing to this unexpected correlation may include the significant demands of academic life [43, 44], isolation within specialized disciplines [45], financial strains [46], and difficulties transitioning to higher education [47]. Stigma surrounding mental health in academic environments may further compound these stressors. Moreover, individuals with higher education levels may have greater awareness of mental health issues and better access to healthcare services, leading to a higher rate and earlier diagnosis of depression compared to less educated individuals who might remain undiagnosed due to limited access or awareness [8]. Thus, addressing these specific stressors and ensuring accessible mental health services for all individuals are essential steps in effectively managing depression in higher education settings.

Medical comorbidities were also a key factor contributing to depression risk, with diabetes and FLD identified as independent predictors. The correlation between diabetes and depression is well-established, with diabetes consistently identified as a significant predictor for the onset of depressive disorders. For instance, Anderson et al. reported that people diagnosed with diabetes are twice as likely to develop depression compared to non-diabetic counterparts [48]. The daily management demands of diabetes, including strict glucose monitoring, medication adherence, and dietary restrictions, likely exacerbate emotional distress and depressive symptoms [49]. Similarly, FLD—a condition characterized by excessive hepatic fat accumulation—has been increasingly linked to depression [50–52]. The metabolic disruptions and inflammatory processes associated with FLD may alter neurotransmitter activity, particularly serotonin, which is crucial for mood regulation [50, 53, 54]. These findings underscore the need to integrate physical and mental health care into the clinical management of patients with chronic illnesses.

Of all the predictors examined, the strongest risk factor for depression in our study was having comorbid psychiatric disorders. Shared biological pathways, including inflammatory interactions and neurochemical dysregulation, likely account for this association [55–57]. Inflammatory processes, in particular, are increasingly recognized as pivotal in the pathogenesis of mental illnesses, influencing neurotransmitter activity and exacerbating psychiatric symptoms [58]. This highlights

the complex relationship between mental health disorders and the importance of comprehensive treatment approaches that address overlapping etiologies. Clinically, the presence of psychiatric comorbidities may complicate diagnosis and management, underscoring the need for integrated mental health services and individualized care plans.

Predictors of the age at onset of depression

Our study identified several factors influencing the age at which depression first manifests, offering valuable insights into its timing and determinants. The mean age at depression onset in our population was 39.5 years (median = 38 years), which is notably higher than the global median onset of 30 years reported in a recent meta-analysis [17]. This difference may reflect cultural, socioeconomic, or healthcare-related factors unique to our population.

Educational attainment was a significant predictor, with individuals holding middle school or diploma-level education experiencing depression earlier than those with both lower and higher educational levels. This pattern suggests that academic underachievement or failure to meet social and economic expectations may accelerate depressive symptoms [59]. Factors such as increased academic pressures [60], feelings of inadequacy in competitive environments [61, 62], and social isolation even in the presence of peers [63] may contribute to this trend. These findings emphasize the necessity of customized interventions within educational settings to address the mental health challenges of individuals across all academic levels.

Interestingly, smoking status revealed no significant link between active smoking and depression onset. However, passive smokers were found to experience a later onset of depression compared to non-smokers. While passive smoking is associated with systemic inflammation and oxidative stress—both linked to depression [64, 65]—the delayed onset observed here may reflect psychosocial contexts. For instance, secondhand smoke exposure might occur in close-knit familial or social environments that provide emotional and social support, delaying the manifestation of depressive symptoms. These findings call for further investigation into the nuanced association between passive smoking and mental health.

Opioid use emerged as another significant factor, associated with an earlier onset of depression. This finding aligns with evidence suggesting that opioids disrupt mood regulation through neurobiological mechanisms, including HPA axis dysregulation and alterations in opioid receptor pathways [66]. Beyond physiological effects, opioids often exacerbate social and psychological stressors, such as isolation, financial strain, and legal issues, which can further accelerate depressive symptoms [67, 68]. Public health efforts should prioritize addressing opioid misuse to reduce its mental health burden.

Comorbid mental disorders were identified as the strongest predictor of earlier depression onset, consistent with the findings of prior research [69]. Shared genetic predispositions and overlapping neurobiological pathways likely explain this association [70–72]. Moreover, the chronic stress of managing a mental illness may amplify feelings of hopelessness and despair, triggering depressive symptoms earlier in life [73]. These results highlight the critical need for early identification and comprehensive care for individuals with psychiatric comorbidities.

Interestingly, chronic physical illnesses such as hypertension, CVD, and stroke were associated with a delayed onset of depression. While previous studies have identified these conditions as risk factors for depression [74–77], our findings suggest they may instead influence its timing. A potential explanation involves medications commonly prescribed for these illnesses, such as angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers [78], statins [79], glucagon-like peptide-1 receptor agonists (GLP-1RAs) [80], and metformin [81], which have demonstrated antidepressant properties. Furthermore, the structured routines and social support inherent in chronic disease management programs may enhance a sense of purpose and control, acting as protective factors against depression [82]. However, due to the cross-sectional design of our study, causality cannot be established, and further longitudinal research is needed.

Finally, we observed a negative correlation between EI and the age of depression onset, indicating that higher energy consumption is linked to earlier depressive episodes. This finding supports evidence that high-caloric diets contribute to systemic inflammation, a key mediator of depression [83]. Elevated energy intake is often related to increased levels of pro-inflammatory markers like leptin and C-reactive protein (CRP), both implicated in depressive symptoms [84]. Additionally, inflammatory dietary patterns in childhood have been shown to elevate the risk of developing depression in early adulthood [85]. These results underscore the importance of dietary interventions as modifiable risk factors in preventing depression, particularly among at-risk populations.

Clinical implications

The findings of the present study offer valuable insights for shaping mental health interventions in rural settings. Identifying key sociodemographic and clinical predictors of depression, as well as factors influencing its age of onset, can guide targeted screening and early intervention strategies. For instance, heightened attention should

be given to individuals with psychiatric and medical comorbidities, those experiencing unemployment, or facing educational pressures. These insights may inform the allocation of resources, support the integration of mental health services within primary care, especially through the family medicine program, and contribute to developing culturally tailored preventive strategies aimed at high-risk rural populations.

Limitations and strengths

This study is subject to several important limitations. First, cultural taboos may have led to underreporting of certain behaviors, particularly alcohol consumption, which could affect the accuracy of our findings. Second, the study did not account for unmeasured confounders such as genetic predispositions, environmental exposures, or early-life stressors, which could influence the age of depression onset. Third, certain potentially relevant demographic variables such as marital status, parental status, number of children, living arrangements, and religious beliefs were not available in the dataset extracted from the cohort. Fourth, the relatively smaller number of depressed participants compared to non-depressed individuals, though consistent with expected prevalence rates, may slightly limit the generalizability of subgroup findings. Lastly, the cross-sectional nature restricts the ability to determine causal relationships, as it lacks temporal sequencing. For instance, while we explored factors associated with the age at depression onset, we cannot confirm whether these factors preceded or resulted from depressive symptoms. To address this, future longitudinal studies with extended follow-up periods are recommended to clarify causal pathways between depression onset and its sociodemographic and clinical determinants.

This study's strength lies in its large sample size, which includes individuals from various socio-economic backgrounds and considers a diverse range of potential covariates and confounders. However, caution should be exercised when generalizing these results to all rural populations in Iran, considering regional variations in socio-economic status, healthcare accessibility, and cultural factors. Additionally, interviews conducted by trained personnel helped to reduce potential biases during data collection.

Conclusion

This study identified key sociodemographic and clinical factors associated with depression and its age of onset in a large rural population. Female sex, unemployment, literacy, diabetes, FLD, and psychiatric comorbidities were found to be significant independent predictors of depression, with psychiatric comorbidities emerging as the strongest contributor. Earlier onset of depression was associated with higher education levels, substance use, psychiatric disorders, and higher EI, while later onset was linked to chronic conditions such as hypertension, CVD, and stroke. These findings suggest complex interactions between individual characteristics, health status, and lifestyle behaviors in shaping the experience of depression.

Our results emphasize the urgent need for preventive strategies and mental health services that address both demographic and clinical risk factors, particularly in rural populations where resources may be limited. Future longitudinal studies are essential to disentangle causal pathways underlying these associations and to evaluate the efficacy of targeted interventions in mitigating depression risk and delaying its onset in vulnerable groups.

Abbreviations

CHD	Coronary Heart Disease
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
CVD	Cardiovascular Disease
FLD	Fatty Liver Disease
BMI	Body Mass Index
MET	Metabolic Equivalent
EI	Energy Intake
FFQ	Food Frequency Questionnaire
SD	Standard Deviation
OR	Odds Ratio
CI	Confidence Intervals
SPSS	Statistical Package for the Social Sciences
GLP-1Ras	Glucagon-like Peptide-1 Receptor Agonists
CRP	C-reactive Protein
ACE	Angiotensin-converting Enzyme
IPAQ	International Physical Activity Questionnaire
PTSD	Post-traumatic Stress Disorder
OCD	Obsessive-compulsive-compulsive Disorder
B	Beta Coefficients
MDD	Major Depressive Disorder

Supplementary Information

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Supplementary Material 1.

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Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author used ChatGPT in order to improve the readability and language of the manuscript. After using this tool/service, the author reviewed and edited the content as needed and take full responsibility for the content of the published article.

Authors' contributions
P.K. and H.K. conceptualized and designed the study and performed the data analysis. A.K., M.K., and M.G. assisted in data collection and management. A.K., P.K., and H.K. drafted the manuscript, and M.K. and M.G. reviewed the manuscript. P.K. supervised the project. All authors read and approved the final manuscript.

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Data availability
The datasets generated and/or analysed during the current study are not publicly available due to the large population included but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Research has been performed in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Fasa University of Medical Sciences on May 18, 2022 (approval code: IR.FUMS.REC.1401.010). Written informed consent was obtained from all participants or their legal guardians if the participant was illiterate. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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