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Individual and integrated indexes of inflammation predicting the risks of mental disorders - statistical analysis and artificial neural network

Shu-Min Huang[1], Fu-Hsing Wu[2†], Kai-Jie Ma[3†] and Jong-Yi Wang[4*]

Abstract

Objective The prevalence of mental illness in Taiwan increased. Identifying and mitigating risk factors for mental illness is essential. Inflammation may be a risk factor for mental illness; however, the predictive power of inflammation test values is unclear. Artificial intelligence can predict the risk of disease. This study was the first to conduct risk prediction based on the combination of individual inflammation test values.

Methods A retrospective longitudinal design was adopted to analyze data obtained from a medical center. Patients were enrolled if they had received blood tests for inflammation. Propensity score matching was employed for within-group comparisons. A total of 231,306 patients were enrolled. A deep neural network model was employed to establish a predictive model.

Results Among inflammation markers, high-sensitivity C-reactive protein concentrations were associated with the greatest risk of mental illness (37.45%), followed by the combination of individual inflammation test values (32.21%). The more abnormal a participant's inflammation values were, the higher the risk of mental illness (aHR = 1.301, $p < .001$). Specifically, high-sensitivity C-reactive protein concentration was the most indicative marker for predicting mental illness. Inflammation markers exhibited certain correlations with the type of mental illness. When the same variables were considered, statistical analysis and the deep neural network had similar results. After feature extraction was incorporated, the performance of the deep neural network model improved (excellent, area under the curve = 0.9162) and could effectively predict the risk of mental illness.

Conclusion Inflammation values could predict the risk of developing mental illnesses in general and the risk of developing certain types of mental illness.

Keywords Inflammation test values, Mental illness, Preventive medicine, Artificial intelligence, Deep learning

†Fu-Hsing Wu and Kai-Jie Ma contributed equally to this work.

*Correspondence:
Jong-Yi Wang
ericwang@mail.cmu.edu.tw
[1]Department of Nursing, China Medical University Hospital, Taichung 404327, Taiwan
[2]Department of Computer Science and Information Engineering, National Taichung University of Science and Technology, Taichung 404336, Taiwan
[3]Department of Public Health, China Medical University, Taichung 406040, Taiwan
[4]Department of Health Services Administration, China Medical University, Taichung 406040, Taiwan

Introduction

According to the World Health Organization, there can be no health without mental health. From the perspective of deep medical management, this study explored whether inflammation was associated with the risk of mental illness.

In clinical practice, the most commonly used inflammatory biomarker is C-reactive protein(CRP), an acute-phase protein that plays a key role in the body's systemic inflammatory response. CRP is widely utilized due to its rapid test results, ease of execution, low cost, and economic efficiency. It serves as a valuable indicator for identifying systemic inflammation in the body, reflecting changes in the inflammatory state, either increasing or decreasing. This makes CRP a highly accessible and commonly used marker in research [1–4]. In recent years, more precise and sensitive tests have been developed to measure lower concentrations of CRP, such as high-sensitivity C-reactive protein(hs-CRP). hs-CRP can accurately quantify lower levels of CRP, making it suitable for monitoring both infectious and non-infectious causes. It serves as a diagnostic and monitoring tool for acute and chronic inflammatory responses. Research has shown that hs-CRP provides more reliable observations than traditional CRP testing [5–8]. Many authoritative global health organizations now recommend the use of CRP to detect undiagnosed diseases, often followed by additional tests such as erythrocyte sedimentation rate(ESR) [3]. Additionally, White blood cell count(WBC) is a common clinical test, and its elevation is highly significant in clinical practice. Therefore, in this study, hs-CRP, ESR, and WBC are included as key inflammatory indicators.

Although inflammation has been associated with mental illness, a causal relationship has not been established [9–12], highlighting the need for further exploration of this topic. This study explored the human body's natural inflammation (excluding those caused by organ, bacterial, or viral infections) by measuring hs-CRP concentrations, ESRs, and WBC concentrations. Previous studies have focused on the associations between inflammation and specific mental illnesses such as depression [5, 7–16] and anxiety disorder [8, 9]. However, these studies have not provided a detailed definition of inflammation, nor have they considered key inflammatory markers such as hs-CRP concentrations, ESRs, and WBC concentrations. Furthermore, these studies typically examine only one type of mental illness at a time, which may lead to biased results. Factors that affect mental health include physical health status [4, 9], demographic characteristics [1], medical provider characteristics [17], and regional characteristics [18]. These factors were accounted for in the present study.

A deep neural network (DNN) is a type of machine learning technique. DNNs make predictions, automatically learn, and are worthwhile research tools [19]. Machine learning techniques can be used to explore the relationship between inflammation and the risk of mental illness [20]. Machine learning can effectively predict the risk of depression and anxiety disorder in patients with inflammation. Machine learning can more accurately predict the risk of depression and anxiety disorder in patients with inflammation than can conventional methods [21]. Artificial intelligence (AI) has been used to predict the risk of mental illness in patients with inflammation. Studies investigating the use of AI to explore associations of inflammation with mental illness have only considered one or 2 types of mental illness and have not used common inflammation biomarkers. The present study obtained data from a clinical database containing patient medical data. The study also developed a DNN model and utilized feature selection algorithms to achieve better accuracy. DNNs are capable of learning complex, non-linear relationships within large datasets, allowing for more precise predictions of mental illness risks based on inflammatory markers. This makes DNNs a particularly useful tool for integrating various inflammatory biomarkers and clinical data to predict mental health outcomes more effectively.

In recent years, a few studies abroad have applied artificial intelligence methods to predict the risk of mental disorders based on inflammatory diseases or inflammatory markers. However, these studies typically focus on only one or two specific types of mental disorders and often analyze a limited range of inflammatory markers, usually single or less common clinical tests. This study, in contrast, utilizes clinical big data from actual medical records, where inflammation tests are performed based on the clinical symptoms and diagnoses made by medical teams. By examining the sequence of disease diagnosis and the timing of inflammation tests, this study provides an in-depth investigation into the predictive value of inflammatory markers for the risk of mental disorders. This approach offers valuable clinical diagnostic reference and employs deep neural network (DNN) technology to explore the role of inflammation tests in predicting mental disorder risks.

Materials and methods

Data sources

This retrospective, longitudinal study conducted secondary data analysis. Data were obtained from the iHi Clinical Research Platform database of a medical center [22]. Electronic medical records for 3 million patients from January 1, 2008, to December 31, 2020, were obtained. Data on hs-CRP concentrations, ESRs, and WBC counts were collected. Mental illness was defined using *International Classification of Diseases, Ninth Edition, Clinical Modification* (*ICD-9-CM*) codes 290 to 319 and

International Classification of Diseases, Tenth Edition, Clinical Modification (*ICD-10-CM*) codes F01 to F99. All types of mental illness were included in this study.

First, the inflammation test results were classified into normal and abnormal groups according to standard reference ranges. After classification, the abnormal group and the normal group were propensity score matched at a ratio of 1:1 based on gender, age, and ECI. A total of 231,306 participants were enrolled. Next, the 231,306 participants were divided into hs-CRP, ESR, and WBC groups, and within each of the three groups, 1:1 propensity score matching with the normal group was conducted based on gender, age, and ECI. In the hs-CRP group, participants were categorized into four subgroups: <1 mg/dL, ≥ 1 ~ < 3 mg/dL, ≥ 3 ~ ≤ 10 mg/dL, and > 10 mg/dL. In the ESR group, the categorization was based on normal reference ranges: for males, the normal range was 0–15 mm/hr, and for females, it was 0–20 mm/hr. These were divided into normal and abnormal subgroups. In the WBC group, participants were divided into three subgroups: $0 \sim < 4*10^3/\mu L$, $\geq 4*10^3/\mu L \sim < 10*10^3/\mu L$, and $\geq 10*10^3/\mu L$. Finally, the abnormal combinations of hs-CRP, ESR, and WBC were merged into a combined group, consisting of 477 participants. The risk of mental illness was explored. Several studies have used an observation period of 1–3 years [23, 24]. The present study used an observation period of 3 years.

「**iHi clinical research platform**」

The iHi Clinical Research Platform is a database established by a large medical center in Taiwan that consists of patient medical data collected over a period of 19 years. The database contains information on patient demographics, medical histories, examination results, and genetic records [22]. The information in the database has undergone de-identification and is confidential. Informed written consent from participants was not required to use the data. This study was approved by the Institutional Review Board (CMUH110-REC2-246(AR-3)).

Inclusion and exclusion criteria

Patients were enrolled if they had undergone blood tests to measure inflammation between 2008 and 2020 and did not have a mental illness. Patients were excluded if their medical records were incomplete ($n = 11,088$), if they were aged 20 years or younger ($n = 842,240$ people), if they were lost to follow-up (i.e., those who failed to receive follow-up assessments yearly for three consecutive years), or if they had a history of mental illness before receiving a diagnosis of inflammation (i.e., those who were diagnosed with a mental illness before January 1, 2010). In total, 231,306 patients were enrolled. Patients were divided into 3 groups: hs-CRP, ESR and WBC groups.

Analytical methods

Data were analyzed using SAS 9.4 for descriptive and inferential statistics. Descriptive statistics, including chi-square tests, were used to explore the relationships between categorical variables. Survival analysis was also conducted in SAS to evaluate time-to-event outcomes. Multinomial logistic regression was performed to examine the association between predictor variables and mental disorder outcomes, while collinearity was measured to ensure the robustness of the model.

For the DNN analysis, the model was developed and optimized in R Studio Version 1.3.1073 using the caret package for training and validation. R was used throughout the entire process, from initial model development, feature selection, training, and optimization, to performing cross-validation. Sensitivity and specificity analyses were also conducted in R to evaluate the model's performance.

Analysis was performed in two stages. In the first stage, the same variables were considered, and sensitivity, specificity, and accuracy were compared. In this stage, 7 predictor variables were used for statistical analysis. In the second stage, the DNN technique was employed. Based on literature review and expert recommendations, feature selection methods were applied to include relevant predictor variables. In this stage, between 10 and 17 predictor variables were used, depending on the feature selection process. Sensitivity, specificity, and accuracy analyses were conducted, and performance was evaluated using area under the curve (AUC) analysis (Fig. 1) [25].

DNN

Variable selection and inclusion/exclusion criteria

In the first stage, the DNN model used the same 7 predictor variables as those employed in the statistical analysis. These variables were selected based on a comprehensive review of the literature, with strong supporting evidence for their relevance in predicting the risk of mental illness based on inflammation markers. These 7 variables include demographic factors (e.g., age, gender), clinical characteristics, and inflammation biomarkers (hs-CRP, ESR, and WBC counts).

In the second stage, the number of variables was expanded to between 10 and 17, with the original 7 variables retained. Additional variables were selected according to expert recommendations, available data from the database, and clinical judgment. These variables were deemed relevant for improving the predictive power of the DNN model, considering both clinical factors and the availability of data. This process ensured that the model accounted for a broader range of factors, thus enhancing its robustness and predictive accuracy.

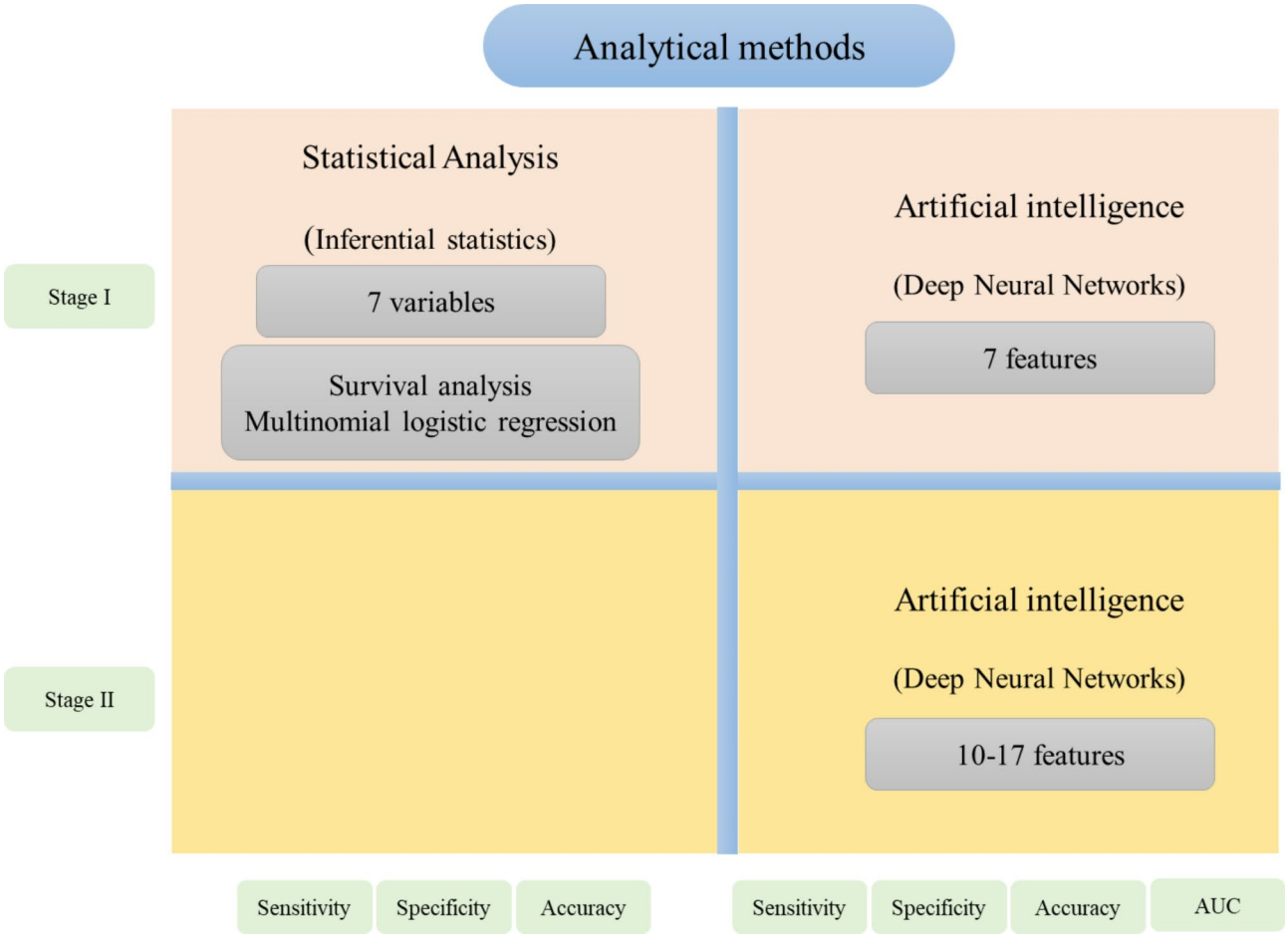

Fig. 1 Analytical methods

Model optimization and configuration

The study performed chi-square tests, survival analysis, and multinomial logistic regression to examine relationships and associations between variables, and collinearity was measured to ensure the robustness of the model.

For the DNN model, it consisted of three hidden layers, with the first, second, and third layers containing 16, 8, and 4 neural nodes, respectively. Two activation functions, namely ReLU and sigmoid, were employed to introduce non-linearity to the model and optimize performance. Various parameters, including epochs, batch size, and the ratio of training to testing samples, were adjusted based on the characteristics of the DNN in each group. Different training-to-testing ratios (1:1, 3:2, 7:3, and 4:1) were used during model training, and the optimal ratio was identified. The loop technique was adopted for process control during training. K-fold cross-validation was performed to assess the model's robustness and generalizability.

Results

In total, 231,306 patients underwent blood tests for inflammation. The hs-CRP, ESR, WBC, and combined test groups comprised 23,901, 26,380, 24,243, and 447 patients, respectively. Mental illness was most prevalent in the hs-CRP group (37.45%), followed by the combined test group (32.21%). Most patients with mental illness had an organic mental disorder and were in the combined test group (12.75%; Table S1).

The average time interval between blood test and the onset of mental illness was as follows: 370.87 days in the hs-CRP group, 624.23 days in the combined test group, 858.62 days in the ESR group, and 1,194.97 days in the WBC group.

The time interval between blood test and the onset of affective psychosis among patients with hs-CRP > 10 mg/dL was 211.52 days. The time interval between blood test and the onset of an anxiety disorder among patients with hs-CRP concentration of ≥ 1 and < 3 mg/dL was 479.35 days. The time interval between blood test and the onset of an organic mental disorder among patients with hs-CRP concentration > 10 mg/dL was 271.79 days. The time

interval between blood test and the onset of other types of mental disorders (including schizophrenia) among patients with hs-CRP concentration > 10 mg/dL was 283.16 days (Fig. 2).

A chi-square test was performed. In all 4 groups, abnormal blood test results were significantly associated with the risk of mental illness ($p < .001$; Tables 1 and 2). Collinearity diagnostics revealed that both residency and degree of urbanization had a variance inflation factor of > 10. Given that residency was considered more relevant to this study, degree of urbanization was not taken into consideration as a factor.

Risk of mental disorder within 3 years

Survival analysis revealed that blood test results were associated with the risk of mental illness (aHR = 1.301, $p < .001$). Specifically, hs-CRP was the most representative marker (Table 3). Among the 4 groups, the combined test group had the highest risk of mental illness (aHR = 3.069, $p = .029$). Patients with multiple known abnormal inflammation test values were at higher risk of developing mental illnesses (58.16%; Table 2). The results of this study revealed that the shortest duration for patients with inflammation to develop mental illness was 1 year. The more abnormal the patients' inflammation test values were, the more likely they were to develop mental illness.

Relationship between inflammation test values and the risk of mental disorders

After calibration, polynomial logistic regression revealed that the types of inflammation markers and the types of mental illness were correlated. The more abnormal a patient's inflammation values were, the higher their risk of organic mental disorders. The WBC group exhibited the highest correlation with organic mental disorders (aOR = 8.074, $p < .001$). The hs-CRP, ESR, and WBC groups had increased risk of affective psychosis, organic mental disorders, and other types of mental disorders ($p < .001$). The hs-CRP and WBC groups had increased risk of anxiety disorders ($p < .001$; Table 3; see Table S3, Table S4, and Table S5 for detailed data).

DNN model

The DNN model was built with three hidden layers: the first layer consisting of 16 neural nodes, the second layer with 8 neural nodes, and the third layer with 4 neural nodes. The activation functions used were ReLU and sigmoid. The model parameters, including epochs, batch size, and the ratio of training to testing samples, were adjusted based on the characteristics of each DNN configuration.

In the first stage, the same 7 predictor variables used in the statistical analysis were applied. The model had three hidden layers, with a 50%-50% training to testing sample ratio. The performance of the model for each inflammation marker was as follows: for the hs-CRP group, sensitivity was 0.5852, specificity was 0.7861, accuracy was 0.6033, and the AUC was 0.7276; for the ESR group, sensitivity was 0.5730, specificity was 0.5387, accuracy was 0.5667, and the AUC was 0.5764; for the WBC group, sensitivity was 0.5979, specificity was 0.7365, accuracy was 0.6173, and the AUC was 0.7163.

In the second stage, the number of predictor variables was increased to 10, and the model's predictive power

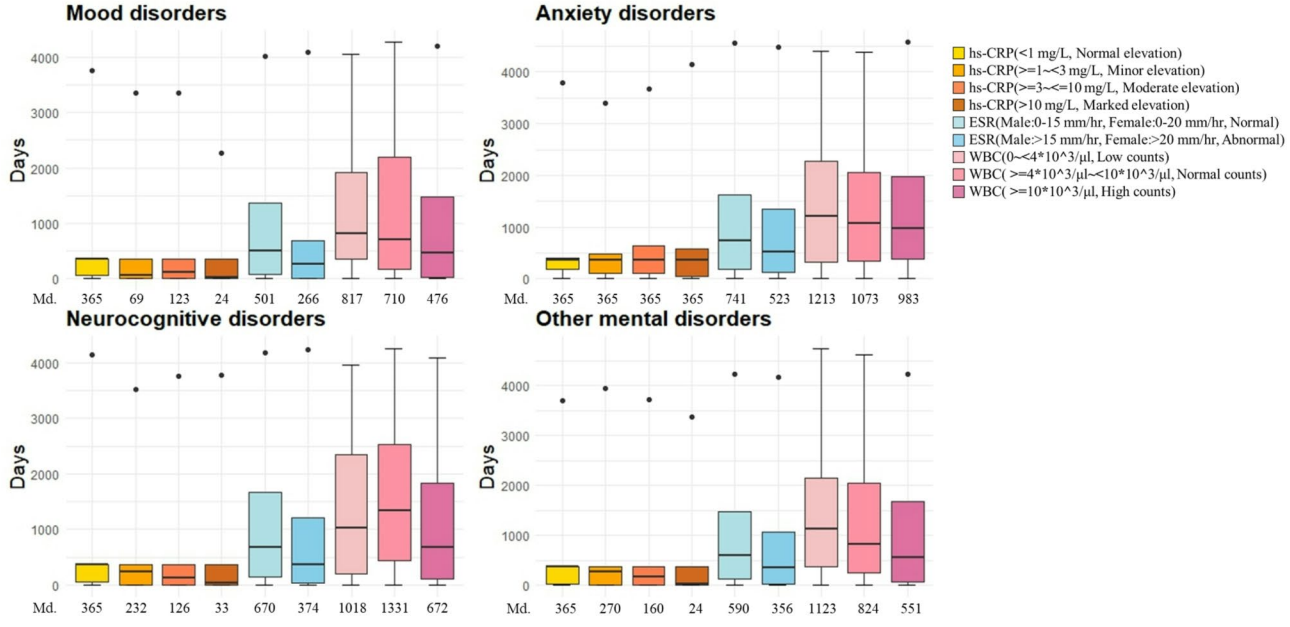

Fig. 2 Time to the onset of each category of mental disorder after inflammation(Follow-up until the data cutoff date)

Table 1 Blood test characteristics of patients with mental illness (*N* = 231,306)

Blood test	Mental disorders		Mood disorders		Anxiety disorders		Neurocognitive disorders		Other mental disorders		Without Mental Disorders		*p*-value
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	
Inflammatory Marker Levels													
hs-CRP concentration													**< 0.001***
< 1 mg/dL	1,716	28.75%	130	2.18%	616	10.32%	395	6.62%	575	9.63%	4,252	71.25%	
>=1 ~ < 3 mg/dL	2,107	35.30%	174	2.92%	631	10.57%	624	10.46%	678	11.36%	3,861	64.70%	
>=3~<=10 mg/dL	2,412	40.22%	255	4.25%	615	10.26%	738	12.31%	804	13.41%	3,585	59.78%	
> 10 mg/dL	2,716	45.51%	262	4.39%	571	9.57%	905	15.16%	978	16.39%	3,252	54.49%	
ESR concentration													**< 0.001***
Normal	3,384	25.66%	255	1.93%	1,293	9.80%	828	6.28%	1,008	7.64%	9,806	74.34%	
Abnormal	3,725	28.24%	363	2.75%	973	7.38%	1,110	8.42%	1,279	9.70%	9,465	71.76%	
WBC concentration													**< 0.001***
0 ~ < $4*10^3$ /μl	806	9.97%	68	0.84%	337	4.17%	133	1.65%	268	3.32%	7,275	90.03%	
>= $4*10^3$/μl ~ < $10*10^3$ /μl	1,522	18.83%	119	1.47%	615	7.61%	269	3.33%	519	6.42%	6,559	81.17%	
>= $10*10^3$ /μl	2,984	36.93%	329	4.07%	1,057	13.08%	599	7.41%	999	12.36%	5,097	63.07%	

significantly improved. The hs-CRP group achieved the highest prediction ability, with an AUC of 0.9162 and specificity of 0.8986. The ESR group had a predictive ability of 85.52%, and the WBC group achieved a prediction ability of 84.51%. For the combined hs-CRP + ESR + WBC group, the DNN model used 17 predictor variables, with sensitivity at 0.4832, specificity at 0.8302, accuracy at 0.5441, and an AUC of 0.7623.

Discussion

Effect of different inflammation test values on risk of mental illness

Whether inflammation test values are correlated to risk of mental illnesses

This study demonstrated that inflammation test values could predict the risk of mental illness. A high value indicated a high risk. Thus, these values could be used as indicators of the risk of mental illnesses. In this study, hs-CRP was identified as the most representative marker. This result is in line with that of other studies: individuals with high CRP concentrations are at increased risk of mental illness [23, 26]. The combined test group had the highest risk of mental illness. Patients with multiple known abnormal inflammation test values are at higher risk of developing mental illnesses.

The severity of inflammation and to what degree the inflammation is being treated may be associated with the risk of mental illness [15, 27]. Increased inflammation values were correlated with the risk of all-cause mortality. Biomarkers generated from inflammation reactions might affect the brain and the central neurotransmitter system and might be correlated to the risk of mental illness [28, 29].

Correlations between inflammation test values and mental illness status

Inflammation test values effectively predicted mental illness status and were correlated with affective psychosis, organic mental disorders, and other types of mental disorders (including schizophrenia). High inflammation test values indicated a high risk of mental illness, especially organic mental disorders (aOR = 8.074). Other studies have not demonstrated this association.

When the human body has inflammation, multiple organs in the body have inflammation, and the biological response of the body is to harm itself. Thus, high inflammation values are associated with a high risk of organic mental disorders. High abnormal inflammation test values are associated with a high risk of depression and other types of mental illness. This positive correlation goes both ways [29, 30].

Table 2 Combined inflammatory tests and risk in patients with mental illness (*N* = 477)

Blood test	With mental disorders		Without mental disorders		*p*-value	aHR	95% CI	*p*-value
	N	%	*N*	%				
hs-CRP + ESR + WBC					**< 0.001***			
All normal"	19	17.43%	90	82.57%		--		
WBC abnormal	8	24.24%	25	75.76%		1.182	0.492–2.843	0.7084
hs-CRP abnormal	9	42.86%	12	57.14%		3.069	1.123–8.389	**0.0288***
ESR abnormal	14	16.67%	70	83.33%		2.695	1.256–5.784	**0.0109***
hs-CRP + WBC abnormal	15	51.72%	14	48.28%		0.822	0.393–1.717	0.6014
ESR + WBC abnormal	8	32.00%	17	68.00%		1.373	0.558–3.377	0.4906
ESR + hs-CRP abnormal	14	29.17%	34	70.83%		1.288	0.609–2.727	0.5078
Both abnormal	57	58.16%	41	41.84%		1.580	0.892-2.800	0.1168

Inflammation test values and the disease progress of mental illness

Having abnormal inflammation test values is associated with a high risk of mental illness. Inflammation test values were correlated with the speed of the manifestation of mental illness, consistent with the findings of other studies [27]. Increased inflammation was positively correlated with the risk of early depression in adults [5]. Patients who experienced inflammation at a younger age were at a 71% increased risk of mental illness compared with their control group counterparts [9].

The hs-CRP group had the highest risk of mental illness and the shortest average time interval between blood test and the onset of mental illness (aHR = 1.301). The combined test group had the highest risk of mental illness (aHR = 3.069), indicating that inflammation test values could serve as indicators that predict the risk of developing mental illness. The WBC group had the youngest mean age of developing mental illnesses (48.47 years).

Comparison and analysis of the results from statistical analysis and the DNN predictive model

In the first stage, under the same variables, statistical analysis and the DNN model performed similarly. In the second part of the first stage, the number of feature extraction items were 10 to 17 (newly added ones were as follows: history of hospitalization, history of surgery, severe illness status, and 8 combinations of individual inflammation test values). The ratios of training and testing data splitting adopted were the original 1:1 and the optimal 7:3. Epochs and batch_sizes were adjusted for training and optimization. After multiple tests, this study selected the model of the optimal performance as the research result. In the second stage, all performances of the DNN predictive model improved. The model reached the "excellent" level (AUC = 0.9162), and the ability to predict the risk of mental illness reached the "success" level (high, ≥ 80%). The model sensitivity was greater than that of statistical analysis, and the model could effectively predict the risk of mental illness (Table S2).

hs-CRP

Inflammatory responses in the body can have a significant impact on the brain, potentially leading to symptoms such as depression and the ineffectiveness of antidepressant treatments. This is because inflammation disrupts key neurotransmitter systems, including serotonin, dopamine, and glutamate pathways, which are crucial for mood regulation, as well as the neurotoxic metabolites produced through the tryptophan-kynurenine pathway [12]. Additionally, neuroimaging studies have shown that the disruption of neurotransmitter systems, combined with inflammation-induced changes in brain circuits, is associated with alterations in the brain's regulation of mechanisms related to anxiety, arousal, and alertness. This, in turn, highlights the complex relationship between inflammation and mental disorders, further supporting the importance of inflammation as a predictor of mental illness risk [13].

In this study, hs-CRP emerged as a key predictor of mental illness, demonstrating a clear association with higher risk of mental disorders, especially organic mental disorders. This result is consistent with the growing body of literature supporting the role of hs-CRP as a biomarker for inflammation-driven mental health risks [31–33]. Specifically, the hs-CRP group exhibited the highest sensitivity and predictive power in the DNN model compared to other inflammation markers such as ESR and WBC, which further solidifies hs-CRP's potential as an important clinical marker for early identification of mental illness risk.

Further analysis revealed that the inclusion of additional features such as patient history (hospitalization, surgery, and major illnesses) enhanced the performance of the DNN model, particularly in predicting mental illness associated with inflammation. This improvement highlights the robustness of hs-CRP as a marker, as well as its relevance when combined with other clinical data to provide a more comprehensive prediction model for mental health outcomes.

This study provides valuable insights into the relationship between inflammation markers and mental

Table 3 Inflammation scores in patients and the risk of developing mental illness

Blood test	With mental disorders / Without mental disorders			Mood disorders / Without mental disorders		Anxiety disorders / Without mental disorders		Neurocognitive disorders / Without mental disorders		Other mental disorders / Without mental disorders	
	aHR	95% CI	*p*-value	aOR(95% CI)	*p*-value	aOR(95% CI)	*p*-value	aOR(95% CI)	*p*-value	aOR(95% CI)	*p*-value
Inflammatory Marker Levels											
hs-CRP concentration											
< 1 mg/dL (ref.)	--	--	--	--	--	--	--	--	--	--	--
>=1~<3 mg/dL	1.125	1.054–1.200	**<0.001***	1.493 (1.179–1.889)	**0.0009***	1.053 (0.933–1.188)	0.4045	1.922(1.664–2.222)	**<0.001***	1.320(1.168–1.492)	**<0.001***
>=3~<=10 mg/dL	1.151	1.080–1.226	**<0.001***	2.368 (1.897–2.955)	**<0.001***	1.018 (0.901–1.150)	0.7747	2.561(2.221–2.953)	**<0.001***	1.723(1.528–1.942)	**<0.001***
> 10 mg/dL	1.301	1.223–1.385	**<0.001***	2.803 (2.245–3.499)	**<0.001***	0.947 (0.836–1.072)	0.3871	3.899(3.387–4.489)	**<0.001***	2.396(2.130–2.695)	**<0.001***
ESR concentration											
Normal (ref.)	--	--	--	--	--	--	--	--	--	--	--
Abnormal	1.244	1.186–1.304	**<0.001***	1.329 (1.126–1.568)	**0.0008***	0.736(0.672–0.805)	**<0.001***	1.339(1.213–1.479)	**<0.001***	1.226(1.121–1.339)	**<0.001***
WBC concentration											
0~<4*10^3 /μl (ref.)	--	--	--	--	--	--	--	--	--	--	--
>=4*10^3/μl~< 10*10^3 /μl	1.005	0.922–1.097	0.9036	1.888(1.394–2.556)	**<0.001***	2.157 (1.874–2.483)	**<0.001***	2.408(1.935–2.997)	**<0.001***	2.180(1.869–2.542)	**<0.001***
>=10*10^3 /μl	1.198	1.103–1.301	**<0.001***	6.537(4.968–8.602)	**<0.001***	5.004 (4.362–5.741)	**<0.001***	8.074(6.571–9.921)	**<0.001***	5.488(4.734–6.361)	**<0.001***

disorders, there are several limitations to consider. First, the data used in this study were obtained from the electronic medical record system, which, while comprehensive, may contain inaccuracies such as missing or misreported data. These inaccuracies could potentially affect the reliability of the findings. Secondly, the data in this study come from a single medical center, which may introduce sample selection bias. To address this limitation, we suggest that future research be conducted across different regions and various types of healthcare institutions to assess the generalizability and applicability of the results. Thirdly, our database lacks data for IL-6 and TNF-α. These markers are also recognized as being associated with mental disorders. Fourthly, we did not perform subgroup analyses of specific types of mental disorders. It is recommended that future studies include such subgroup analyses to better understand the relationship between inflammation markers and specific mental disorders. Fifthly, the "black-box" nature of the DNN model limits its interpretability. Future studies could consider using techniques like SHAP or LIME to improve model transparency and better understand the specific relationships between inflammation markers and mental disorders. Sixthly, as our study relies on large clinical database data, we were unable to compare our model with commonly used clinical tools, such as psychometric scales or existing risk assessment models.

Conclusions

The level of inflammation test values could predict the risk of mental illness and the types of such illness. The concentration of hs-CRP and the combination of individual inflammation test values were indicative. Among the various inflammatory markers, the hs-CRP group exhibited the shortest average time interval to the onset of mental illness (370.87 days), along with a higher incidence of mental disorders (37.45%). As the hs-CRP values increased and the levels became more abnormal, the risk and incidence of mental illness significantly increased. Individuals with hs-CRP > 10 mg/dL exhibited the highest and most significant risk and incidence of mental disorders. The WBC group developed mental illness at the youngest age; this group is at risk for early onset of mental illness and is worthy of attention. After feature items were incorporated, the DNN model could be used in clinical practice to predict the risk of mental illness. Competent authorities should incorporate inflammation as a factor and increase financial incentives for referrals across departments to strengthen the predictive measures for mental illness. Psychiatric medical screening should prioritize populations with multiple abnormal results from inflammation tests, and screening should be conducted no later than 1 year after inflammation is identified to improve mental illness prevention.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-025-06652-3.

Supplementary Material 1

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Author contributions
S.M.H. and J.Y.W. designed and conceptualized the study. F.H.W. and K.J.M. analyzed the data. S.M.H. and K.J.M. drafted the first version of the article. S.M.H. performed the literature search and reviewed the article. All authors contributed substantially to the article and approved the final article for submission. All authors are responsible for the integrity, accuracy, and presentation of the data.

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Data availability
The data that support the findings of this study are available from the China Medical University Hospital, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the corresponding author (Jong-Yi Wang, E-mail: ericwang@mail.cmu.edu.tw) upon reasonable request and with permission of China Medical University Hospital.

Declarations

Ethics approval and consent to participate
In this study, all the research database involving humans were conducted ethically and in accordance with the Declaration of Helsinki. Our study protocols were reviewed and approved by the Institutional Review Board of the China Medical University Hospital (CMUH110-REC2-246). To protect the patients' privacy, all personal identification numbers were encrypted by the China Medical University Hospital before the data were analyzed and released. Therefore, patient informed consent is not required for authorized researchers to access this research database. The researchers of this study are not possible to contact any studied patient for obtaining informed consent. No informed consent form is used in this study. Furthermore, the Institutional Review Board of China Medical University Hospital (CMUH110-REC2-246) also specifically waived the requirement of informed consent.

Competing interests
The authors declare no competing interests.

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