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Relation between sirtuin-1 activity and graft-versus-host disease (GVHD) status post allogeneic haematopoietic stem-cell transplantation (HSCT): Prospective study

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Abstract

Graft-versus-host disease (GVHD) remains one of the major complications after allogeneic bone marrow transplantation (allo-BMT). Acute GVHD (aGVHD) is distinguished by uncontrolled activation, migration, and proliferation of allogeneic donor T cells, as well as their production of pro-inflammatory cytokines in GVHD target organs. This study aimed to investigate the role of sirtuin-1 (sirt-1) in mediating GVHD and the relation between the activity of sirt-1 in T cells and the incidence of GVHD. This two-arm exploratory study was conducted at Ain Shams University over a period of six months. It included patients aged 18 to 65 years of both sexes who had undergone allogeneic stem cell transplantation and were admitted to the hospital with symptoms of acute or chronic GVHD. The study showed significantly elevated serum Sirt-1 levels in GVHD positive patients, supporting its role in GVHD pathogenesis. A cutoff >15.8 provided 73.3% sensitivity and 93.3% specificity for distinguishing GVHD. In conclusion, this study demonstrated that serum Sirt-1 levels are significantly elevated in patients with GVHD following allogeneic hematopoietic stem cell transplantation, highlighting its potential as a diagnostic biomarker with high specificity.

Keywords: Sirtuin-1, GVHD, HSCT.

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Introduction

Graft-versus-host disease (GVHD) remains one of the major complications after allogeneic bone marrow transplantation (allo-BMT). Acute GVHD (aGVHD) is distinguished by uncontrolled activation, migration, and proliferation of allogeneic donor T cells, as well as their production of pro-inflammatory cytokines in GVHD target organs. In contrast, chronic GVHD (cGVHD) pathogenesis involves several immune cell types, including pathogenic T- and B-cell interactions and follicular T helper cell (Th) generation.[1]

Sirtuin-1 (Sirt-1) belongs to the class III histone deacetylase family, which collectively deacetylates a broad range of transcription factors and co-regulators, subsequently resulting in up- or down-regulation of target gene expression. Sirt-1 requires nicotinamide

adenosine dinucleotide as a co-substrate on de-acetylation.[2]

A previous study, addressed the role of Sirt-1 in GVHD induction by employing Sirt-1 conditional knockout mice as well as a pharmacological Sirt-1 inhibitor. Using major histocompatibility complex (MHC)–mismatched and MHC-matched murine BMT models, we found that Sirt-$1^{-/-}$ T cells had a reduced ability to induce acute GVHD (aGVHD) via enhanced p53 acetylation. Sirt-1-deficient T cells also promoted induced regulatory T cell (iTreg) differentiation and inhibited interferon-γ production after allo-BMT. Sirt-1 deletion in iTregs increased Foxp3 stability and restrained iTreg conversion into pathogenic T cells.[3]

Mechanistic studies revealed that Sirt-1 deficiency in T cells enhanced splenic B-cell reconstitution and reduced follicular T helper cell development. Sirt-1 deficiency in T cells modulated donor B-cell responses reducing both B-cell activation and plasma cell differentiation. In addition, therapeutic Sirt-1 inhibition could both prevent cGVHD and reduce established cGVHD. In conclusion, Sirt-1 is a promising therapeutic target for the control of aGVHD and cGVHD pathogenesis and possesses high potential for clinical application.[4,, 5] This study aimed to investigate the role of sirt-1 in mediating GVHD and the relation between the prevalence of sirt-1 in T cells and the incidence of GVHD.

Patients and Methods

This cross sectional study was performed during 6 months period at Ain Shams University. The study included individuals with 18- 65 years old, of both sexes. They were admitted to the hospital with symptoms of acute and chronic GVHD and had allogeneic stem cell transplantation after different types of conditioning treatments. They included 15 patients with GVHD, 15 patients in controlled arm post HSCT without GVHD and 10 subjects in the control group. Exclusion criteria included patients with autologous transplantation and age less than 18 or more than 65 years.

All the patients underwent full history taking, full examination, complete blood count (CBC) with differential count, kidney and liver function tests, detection of GVHD according to the recent guidelines and Sirt-1 activity assessment by an enzyme linked immunoassay (ELISA).[6]

Statistical Analysis

Data were analyzed using the Statistical Program for Social Science (SPSS) version 24. Qualitative data are expressed as frequency and percentage. Quantitative data are expressed as mean ±SD for normally distributed data or median (IQR) for non-normally distributed data. The Mean (average): the central value of a discrete set of numbers, specifically the sum of values divided by the number of values. Standard deviation (SD): is the measure of dispersion of a set of values. A low SD indicates that the values tend to be close to the mean of the set, while a high SD indicate that the values are spread out over a wider range. The Median: The middle number; found by ordering all data points and picking out the one in the middle (or if there are two middle numbers, we took the mean of those two numbers). IQR (inter-quartile range): is a measure of statistical dispersion, which is the spread of the data. It is defined as the difference between the 75th and 25^{th} percentiles of the data. A *p*-value < 0.05 was considered significant.

Results

Our study showed no statistically significant difference (*p*-value = 0.209) between studied groups as regard age. In GVHD positive patients, mean age was 41.8 ± 11.5 with age range of 26 – 62 years. In GVHD negative patients, mean age was 34.9 ± 9.6 with age range of 19 – 51 years. In Control group, mean age was 42.3 ± 15.7 with age range of 19 – 62 years.

It was also shown that there was no statistically significant difference (*p*-value = 0.911) between studied groups as regard sex. In GVHD positive patients, there were 9 males (60%) and 6 females (40%). In GVHD negative patients, there were 10 males (66.7%) and 5 females (33.3%). In Control group, there were 8 males (66.7%) and 4 females (33.3%) as shown in (Table 1).

Table 1. Comparison of age and sex between the studied groups.

		Groups						*p*-value
		GVHD positive (n = 15)		GVHD negative (n = 15)		Control (n = 12)		
Age (years)	Mean ±SD	41.8 ± 11.5		34.9 ± 9.6		42.3 ± 15.7		NS^F
	Range	26 - 62		19 - 51		19 – 62		
Sex	Male	9	60%	10	66.7%	8	66.7%	NS^{X2}
	Female	6	40%	5	33.3%	4	33.3%	

X^2: Chi-square test. F: F value of ANOVA test., SD (standard deviation). $p > 0.05$ is not significant (NS).
GVHD: Graft-versus-host disease.

Using the receiver operating characteristic (ROC) curve analysis, it was shown that serum Sirt-1 can be used to discriminate GVHD patients at a cutoff level of > 15.8, with 73% sensitivity, 93.3% specificity, 91.7% positive predictive value (PPV) and 77.8% negative predictive value (NPV) (at an Area under curve [AUC] = 0.8 & *p*-value = 0.001).as shown in (Table 2) and(Figure: 1).

Table 2. Diagnostic performance of serum Sirt-1 in discrimination of GVHD patients.

	Cut off	AUC	Sensitivity	Specificity	PPV	NPV	*p*-value
Sirt-1	> 15.8	0.8	73.3%	93.3%	91.7%	77.8%	0.001

PPV: positive predictive value. AUC: Area under curve. NPV: negative predictive value. $p \leq 0.05$ is significant.

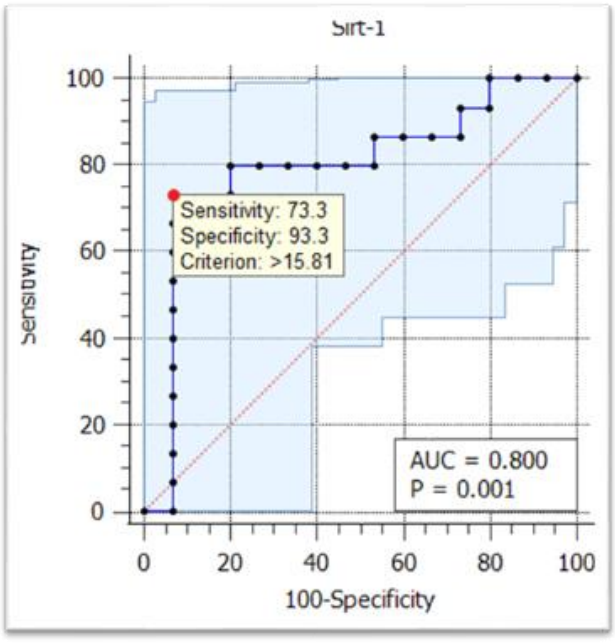

Figure 1. Receiver operating characteristic (ROC) curve of serum sirtuin-1 (Sirt-1) in discrimination of GVHD patients.

As regard CBC, Table 3, shows that there was no statistically significant difference between hemoglobin (Hb), total leukocyte count (TLC), platelets (PLTs) and Blast count % in the GVHD positive patients and GVHD negative patients (*p*-values of *p*=0.450, *p*=0.225, *p*=0.338 and *p*=0.231, respectively).

As regard kidney function tests (KFTs), the same table shows no statistically significant difference between GVHD positive patients and GVHD negative patients, except for uric acid (UA), there was statistically significant increase of UA in GVHD positive patients (mean = 5.91 ± 1.26, range = 4.2 – 8.1) when compared with GVHD negative patients (mean = 4.77 ± 1.07, range = 3.4 – 6.8) (p= 0.012).

As regard liver function tests (LFTs), the same table shows no statistically significant difference in LFTs between GVHD positive patients and GVHD negative patients except for alanine transaminase (ALT). ALT was significantly increased in GVHD positive patients (mean = 90.1 ± 82.2, range = 14 – 323) when compared with GVHD negative patients (mean = 38.1 ± 29.3, range = 10 – 136) (p= 0.028).

As regard Minimal Residual Disease (MRD) & ECOG performance score, Table 3 shows that there was no statistically significant difference in MRD between GVHD positive patients and GVHD negative patients.

There was no statistically significant difference in the ECOG score between GVHD positive patients and GVHD negative patients.

Table 3. Comparison of studied data between the GVHD groups.

		GVHD		p-value[T]
		Positive (N = 15)	Negative (N = 15)	
Hemoglobin (g/dl)	Mean ±SD	12.4 ± 1.3	12.8 ± 1.7	NS
	Range	11 - 15.2	10.1 - 15.2	
Total Leukocytic Count (x10^3/μl)	Mean ±SD	6 ± 2.1	5.2 ± 1.7	NS
	Range	3.6 - 9.5	0.2 - 7.79	
Platelets (x10^3/μl)	Mean ±SD	234.6 ± 73.9	208.5 ± 72.6	NS
	Range	132 - 358	23 - 352	
Blast count (%)	Mean ±SD	1.3 ± 0.65	1.07 ± 0.27	NS
	Range	0 - 2.5	1 - 2	
BUN	Mean ±SD	14.5 ± 3.4	16.1 ± 4.1	NS
	Range	9 - 22	10 - 25	
Creatinine(mg/dl)	Mean ±SD	0.87 ± 0.33	0.81 ± 0.25	NS
	Range	0.6 - 1.69	0.5 - 1.5	
Uric Acid (mg/dl)	Mean ±SD	5.91 ± 1.26	4.77 ± 1.07	0.012
	Range	4.2 - 8.1	3.4 - 6.8	
Total Bilirubin (mg/dl)	Mean ±SD	1.03 ± 1.15	0.67 ± 0.21	NS
	Range	0.1 - 4.2	0.3 - 1	
Direct Bilirubin (mg/dl)	Mean ±SD	0.57 ± 1.08	0.16 ± 0.08	NS
	Range	0.1 - 4.1	0.1 - 0.4	
Total Protein (g/dl)	Mean ±SD	7 ± 0.7	7.3 ± 0.4	NS
	Range	5.1 - 8.5	6.4 - 7.9	
Albumin (g/dl)	Mean ±SD	3.9 ± 0.5	4.2 ± 0.4	NS
	Range	2.7 - 4.6	3.6 - 4.9	

Table 3. Continued.

		GVHD		*p*-value[T]
		Positive (N = 15)	Negative (N = 15)	
AST (U/L)	Mean ±SD	74.2 ± 73.5	39.7 ± 47.8	NS
	Range	10 - 262	12 - 207	
ALT (U/L)	Mean ±SD	90.1 ± 82.2	38.1 ± 29.3	0.028
	Range	14 - 323	10 - 136	
Alkaline phosphatase (U/L)	Mean ±SD	128.5 ± 57.6	112.5 ± 50.8	NS
	Range	76 - 299	67 - 229	
MRD	Mean ±SD	0.15 ± 0.11	0.16 ± 0.27	NS
	Range	0.1 - 0.5	0 - 1	
ECOG performance score	Mean ±SD	0.67 ± 0.62	0.27 ± 0.8	NS
	Range	0 - 2	0 - 3	

T: Independent sample T test, Alanine transaminase (ALT), Aspartate transaminase (AST), Minimal Residual Disease (MRD). Eastern Cooperative Oncology Group Performance (ECOG). $p > 0.05$ is not significant (NS).
GVHD: Graft-versus-host disease. BUN: blood urea nitrogen.

When comparing the relation between sirt 1 and the type of conditioning treatment, there was no statistically significant difference with (*p*-value = 0.558). In GVHD positive patients, there were 5 patients (33.3%) on TBI/CY, 8 patients (53.3%) on BU/FLU and 2 patients (13.3%) on BU/FLU/CY. In GVHD negative patients, there were 3 patients (20%) on TBI/CY, 8 patients (53.3%) on BU/FLU and 4 patients (26.7%) on BU/FLU/CY. (Table 4)

Table 4. Comparison of conditioning regimen between GVHD groups.

		GVHD				*p*-value
		Positive (N = 15)		Negative (N = 15)		
Conditioning regimen	TBI/CY	5	33.3%	3	20%	NS[X2]
	BU/FLU	8	53.3%	8	53.3%	
	BU/FLU/CY	2	13.3%	4	26.7%	

X^2: Chi-square test. TBI: Total body irradiation BU:buslfan, FLU:Flaudara, GVHD: Graft-versus-host disease.
CY: Cyclophosphamide. $p > 0.05$ is not significant (NS).

As regard GVHD status, it was active in 9 patients (60%) and quiescent in 6 patients (40%). As regard GVHD type, it was chronic GVHD in 14 patients (93.3%) and acute on top of chronic GVHD in 1 patient (6.7%). As regard affected organs, it was hepatic in 11 patients (73.3%), pulmonary in 2 patients (13.3%) and skin in 4 patients (26.7%). As regard GVHD grade, it was mild in 13 patients (86.7%) and moderate in 2 patients (13.3%). As regard received treatment, Ruxolitinib was used in 6 patients (40%), Ruxolitinib + CNIs were used in 4 patients (26.7%), CNIs + steroids were used in 3 patients (20%) and Ruxolitinib + CNIs + Steroids were used in 2 patients (13.3%) while Ruxolitinib + Steroids were not used. (Table 5)

Table 5. Description of clinical and treatment data in the 15 GVHD positive patients.

		GVHD positive patients (N = 15)	
GVHD status	Active	9	60%
	Quiescent	6	40%
GVHD type	Chronic	14	93.3%
	Acute on top of chronic	1	6.7%
Organ affected	Hepatic	11	73.3%
	Pulmonary	2	13.3%
	Skin	4	26.7%
Grade	Mild	13	86.7%
	Moderate	2	13.3%
Treatment	Ruxolitinib	6	40%
	Ruxolitinib + CNIs	4	26.7%
	Ruxolitinib + Steroids	0	0%
	CNIs + steroids	3	20%
	Ruxolitinib + CNIs + Steroids	2	13.3%

GVHD: Graft-versus-host disease.

In the GVHD positive patients, there were several statistically significant correlations. These included a statistically significant negative correlation (r = - 0.62, *p*= 0.015) between Sirt-1 and total protein (TP). Also, there was a statistically significant positive correlation (r = 0.54, *p* = 0.036) between Sirt-1 and alanine aminotransferase (ALT). And, there was no statistically significant correlation between Sirt-1 and other studied parameters

In the GVHD negative patients, there were several statistically significant correlations. These included statistically significant positive correlation between Sirt-1 and PLTs (r = 0.54, *p*= 0.039): statistically significant positive correlation between Sirt-1 and BUN (r = 0.54, *p*= 0.037); statistically significant positive correlation between Sirt-1 and creatinine (r = 0.75, *p*= 0.001) However, there was no statistically significant correlation between Sirt-1 and other studied parameters. (Table 6)

Table 6. Correlation between Sirt-1 and other studied parameters in the GVHD groups.

Sirt-1	GVHD positive		GVHD negative	
	r	*p*-value	r	*p*-value
Age	0.13	NS	-0.08	NS
Hb	-0.21	NS	0.07	NS
TLC	-0.17	NS	0.33	NS
PLTs	-0.30	NS	0.54	0.039
BMA after	0.39	NS	0.02	NS
BUN	-0.17	NS	0.54	0.037
Creatinine	0.30	NS	0.75	0.001
Uric acid	-0.05	NS	0.49	NS

Table 6. Continued.

Sirt-1	GVHD positive		GVHD negative	
	r	*p*-value	r	*p*-value
Total Bilirubin	0.42	NS	-0.09	NS
Direct Bilirubin	0.45	NS	0.16	NS
Total protein	-0.62	0.015	-0.21	NS
Albumin	-0.48	NS	0.14	NS
AST	0.44	NS	0.04	NS
ALT	0.54	0.036	0.03	NS
Alk ph	0.004	NS	-0.24	NS
MRD	0.04	NS	-0.09	NS
ECOG score	0.02	NS	-0.16	NS

(r): Pearson correlation coefficient. $p > 0.05$ is not significant (NS). GVHD: Graft-versus-host disease. BUN: blood urea nitrogen; Alanine transaminase (ALT), Aspartate transaminase (AST), Minimal Residual Disease (MRD). Alk ph:Alkaline phosphatase. Hemoglobin (Hb), total leukocyte count (TLC), platelets (PLTs)

The study showed a statistically significant difference (*p*-value = 0.027) between the level of Sirt-1 and the studied group. In GVHD positive patients, mean Sirt-1 was 24.6 ± 14.8 with median Sirt-1 of 22.2 (12.5 – 42.8). In GVHD negative patients, mean Sirt-1 was 10.8 ± 11.9 with median Sirt-1 of 10.4 (4.1 – 11.9). In Control group, mean Sirt-1 was 15.9 ± 18.02 with median Sirt-1 of 8.3 (1.16 – 33.7). (Table 7)

Table 7. Comparison of Sirt-1 between the studied groups.

		Groups			*p*-value
		GVHD positive (n = 15)	GVHD negative (n = 15)	Control group (n = 12)	
Sirt-1	Mean ±SD	24.6 ± 14.8	10.8 ± 11.9	15.9 ± 18.02	0.027^{KW}
	Median (IQR)	22.2 (12.5 – 42.8)	10.4 (4.1 – 11.9)	8.3 (1.16 – 33.7)	

KW: Kruskal Wills test. GVHD: Graft-versus-host disease. $p \leq 0.05$ is significant.

Discussion

GVHD remains a major complication following allogeneic HSCT, significantly impacting morbidity and mortality among transplant recipients.[7] It arises when donor-derived immune cells, particularly T lymphocytes, recognize host tissues as foreign and initiate an immune-mediated attack.[8]

This condition can be classified into acute and chronic forms, each with distinct clinical features and pathophysiological mechanisms. Despite advances in immunosuppressive therapies and transplant protocols, GVHD continues to challenge clinicians due to its complex immunology and unpredictable course. Identifying reliable biomarkers that can predict, diagnose, or monitor GVHD is crucial for improving patient outcomes and tailoring individualized treatment strategies.[9]

Sirt-1, a nicotinamide adenine dinucleotide (NAD+)-dependent histone deacetylase, has emerged as a key regulator of immune responses, inflammation, and cellular metabolism.[10] It influences T cell differentiation, cytokine secretion, and the stability of regulatory T cells, all of which are integral to the immune tolerance required post-HSCT.[11]

This study aimed to investigate the role of Sirt-1 in mediating GVHD and the relation between the activity of Sirt-1 in T cells and the incidence of GVHD. Our findings demonstrated that serum (Sirt-1) levels were significantly higher in GVHD-positive patients compared to

GVHD-negative ones (24.6 ± 14.8 vs. 10.8 ± 11.9, p = 0.015). This elevation suggests a strong association between Sirt-1 activity and GVHD pathogenesis. Sirt-1, a NAD+-dependent histone deacetylase, is known for its involvement in immunoregulation and inflammation control.

The study by Xu et al., 2018, provided mechanistic insight into this association by showing that Sirt-1 deficiency in CD4+ T cells led to over activation of the PI3K/Akt/mTOR and signal transducer and activator of transcription 3 signaling pathways both implicated in immune cell hyper activation during acute GVHD. The study further identified interleukin (IL)-1β-driven transforming growth factor-β-activated kinase 1 signaling as a cause of Sirt-1 depletion, resulting in exaggerated T cell responses. These mechanistic findings provided a strong biological basis for the elevated Sirt-1 levels observed in our GVHD-positive cohort, possibly representing a compensatory or disease-reflective up-regulation.[12]

Although our study showed elevated Sirt-1 levels in GVHD-positive patients, no statistically significant difference was observed between GVHD-positive patients and normal controls. This could be attributed to variability in immune reconstitution after HSCT or the presence of subclinical inflammation even in control subjects. Nonetheless, the ROC curve analysis showed that a Sirt-1 cutoff of >15.8 provided 73.3% sensitivity and 93.3% specificity (p = 0.001) for identifying GVHD cases. This high specificity makes Sirt-1 particularly valuable for confirming GVHD in ambiguous cases, reducing unnecessary treatment interventions. The study by Li et al., 2020, similarly underscored the importance of integrating epigenetic regulators such as histone deacetylases (including Sirt-1) into the GVHD diagnostic and therapeutic landscape, reinforcing its clinical potential.[13]

In terms of organ-specific involvement, we identified a significant positive correlation between Sirt-1 and ALT levels (r = 0.54, p = 0.036), suggesting liver inflammation as a key contributor to elevated Sirt-1. This correlation aligns with the observation that hepatic involvement was the most common organ manifestation in our GVHD-positive cases. The findings are consistent with those of Mohamed et al., 2021, who reviewed the role of metabolic regulators in GVHD, noting that Sirt-1 modulates injury responses in the liver and gastrointestinal tract two commonly affected sites in GVHD.[14] These insights support the interpretation of Sirt-1 as both a marker and a potential effector in hepatic immune injury.

A noteworthy inverse correlation was found between Sirt-1 and total protein levels (r = -0.62, p = 0.015), which may reflect catabolic states or protein-losing enteropathy frequently observed in chronic GVHD. These changes in protein homeostasis can be driven by systemic inflammation and immune-mediated tissue damage. The study by Gail et al., 2023, provided a deeper understanding of the chronic GVHD microenvironment, emphasizing the multifaceted cellular interactions and extracellular vesicle signaling that promote persistent tissue remodeling, fibrosis, and immune activation all of which may influence Sirt-1 expression.[15]

Additional laboratory findings revealed significantly elevated uric acid and ALT in GVHD-positive patients, further supporting the presence of metabolic stress and liver dysfunction. The review by Rasha et al., 2020, offers insight into how Sirt-1 regulates immuno-metabolism and oxidative stress responses across different organ systems. They describe Sirt-1 as a "versatile regulator" in immuno-endocrine balance, with up-regulation in inflammatory states reflecting its role in cellular adaptation and stress resilience.[16]

Interestingly, among GVHD-negative patients, Sirt-1 levels correlated positively with platelet count, BUN, and creatinine, suggesting a link between Sirt-1 and systemic physiological processes like renal function and hematopoietic activity. The study by Chen et al., 2015, emphasized Sirt-1's role as a metabolic sensor in immune cells, controlling oxidative metabolism and cytokine profiles. These correlations suggest that even in the absence of GVHD, Sirt-1 may act as a broader marker of immune and organ function recovery post-transplant.[4]

Despite elevated Sirt-1 levels in GVHD-positive patients, no significant difference was observed between active and quiescent disease states (p = 0.776). This may indicate persistent

Sirt-1 activity in chronic GVHD regardless of clinical fluctuations, possibly due to sustained fibrotic and autoimmune processes. The study by Saidu et al., 2020, discussed how chronic GVHD is characterized by prolonged immune dysregulation and remodeling of affected tissues, which may account for the observed consistency in Sirt-1 levels across disease phases.[17]

Therapeutically, a significant proportion of GVHD-positive patients in our study received Ruxolitinib a Janus Kinase 1 (JAK1)/2, inhibitor known for suppressing inflammatory signaling. While we did not directly evaluate its effect on Sirt-1, the study by Mohamed et al., 2021, pointed out to the intersection between metabolic and epigenetic regulators and JAK-STAT pathways.[14] It is plausible that immunosuppressive therapies could alter Sirt-1 expression or activity, which should be addressed in future studies evaluating Sirt-1 as a biomarker or therapeutic target.

Importantly, there were no statistically significant differences in demographic or baseline clinical variables (e.g., age, sex, conditioning regimen, malignancy type) between GVHD-positive and -negative groups. This supports the internal validity of our findings and suggests that Sirt-1 differences are likely linked to GVHD status rather than background factors.

In conclusion, this study demonstrated that serum Sirt-1 levels are significantly elevated in patients with GVHD following allogeneic HSCT, highlighting its potential as a diagnostic biomarker with high specificity. The positive correlation of Sirt-1 with liver enzymes and its association with hepatic involvement suggest a role in GVHD-related organ damage, particularly in chronic cases. While no significant correlation was found with disease activity status, the findings support further investigation into Sirt-1 as a marker of GVHD presence and severity.

Author Contributions

All authors contributed to the study conception and design. Data collection was performed by ASFD. Material preparation, data analysis was performed by IMK and RGA and NAN. The first draft of the manuscript was written in collaboration between by IMK and RGA and MM. All authors commented on previous versions of the manuscript and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

the study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Ain Shams University (approval: FMASU MS 59/2022).

Informed consent

A written informed consent was obtained from each participant before being included in the study.

References

1. Zeiser R, Sarantopoulos S, Blazar BR. (2018). B-cell targeting in chronic graft-versus-host disease. *Blood.* 29: 131(13):1399-1405.

2. Drazic, A., Myklebust, L. M., Ree, R., et al. (2016). The world of protein acetylation. *Biochimica et Biophysica Acta (BBA)-proteins and proteomics,* 1864(10):1372-1401.

3. Daenthanasanmak, A., Iamsawat, S., Chakraborty, P., et al. (2019). Targeting Sirt-1 controls GVHD by inhibiting T-cell allo-response and promoting Treg stability in mice. Blood, *The Journal of the American Society of Hematology*, 133(3):266-279.

4. Chen, X., Lu, Y., Zhang, Z., et al. (2015). Intercellular interplay between Sirt1 signalling and cell metabolism in immune cell biology. Immunology, 145(4):455-467.

5. Huang FT, Sun J, Zhang L, et al. (2019). Role of SIRT1 in hematologic malignancies. *J Zhejiang Univ Sci B.* 20(5):391-398.

6. Lee SJ, Williams KM, Sarantopoulos S et al. (2025). NIH Chronic Graft-Versus-Host Disease Consensus Conference 2025 Update. *Transplant Cell Ther.* 31(9):678.e1-678.e16

7. Pellegrini, M., Bernabei, F., Barbato, F., et al. (2021). Incidence, risk factors and complications of

ocular graft-versus-host disease following hematopoietic stem cell transplantation. *American Journal of Ophthalmology,* 227: 25–34.

8.- Inoue, Y., Okinaka, K., Fuji, S., et al. (2021). Severe acute graft-versus-host disease increases the incidence of blood stream infection and mortality after allogeneic hematopoietic cell transplantation: Japanese transplant registry study. *Bone Marrow Transplantation,* 56(9):2125–2136.

9. Watkins, B., & Williams, K. M. (2022). Controversies and expectations for the prevention of GVHD: a biological and clinical perspective. *Frontiers in Immunology,* 13:1057694.

10. Santos L, Benitez-Rosendo A, Bresque M. et al. (2023). Sirtuins: the NAD+-dependent multifaceted modulators of inflammation. *Antioxidants & Redox Signaling,* 39:1185–1208.

11. Yang, Y., Liu, Y., Wang, Y., et al. (2022). Regulation of SIRT1 and its roles in inflammation. *Frontiers in Immunology*, 13:831168.

12. Xu, Y. J., Chen, F. P., Chen, Y., et al. (2018). A possible reason to induce acute graft-vs.-host disease after hematopoietic stem cell transplantation: Lack of Sirtuin-1 in CD4+ T cells. *Frontiers in Immunology,* 9:3078.

13. Li, A., Abraham, C., Wang, Y., & Zhang, Y. (2020). New insights into the basic biology of acute graft-versus-host disease. *Haematologica*, 105(11):2540–2547.

14. Mohamed, F. A., Thangavelu, G., Rhee, S. Y., et al. (2021). Recent metabolic advances for preventing and treating acute and chronic graft versus host disease. *Frontiers in Immunology*, 12:757836.

15. Gail, L. M., Schell, K. J., Łacina, P., et al. (2023). Complex interactions of cellular players in chronic graft-versus-host disease. *Frontiers in Immunology*, 14: 1199422.

16. Rasha F, Mims BM, Castro-Piedras I. et al. (2020). The versatility of sirtuin-1 in endocrinology and immunology. *Frontiers in Cell and Developmental Biology,* 8: 589016.

14. Saidu, N. E. B., Bonini, C., Dickinson, A., et al. (2020). New approaches for the treatment of chronic graft-versus-host disease: Current status and future directions. *Frontiers in Immunology*, 11:578314.