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Original Study

Assessment of Lysosome-Associated Membrane Protein (LAMP5) in Newly Diagnosed Multiple Myeloma Patients and Correlation to Clinical Outcome

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Abstract

Introduction: Lysosome-associated membrane protein 5(LAMP5) is one of the glycosylated proteins which are implicated in several different features of cell biology and can impact cellular processes for instance phagocytosis, autophagy, lipid transference, and aging. Interestingly, it has a significant role in cancer progression, metastatic spread and aggressiveness. It has been reported to be significantly expressed in many hematopoietic malignancies as leukemias and Multiple Myeloma (MM).

Objectives: This study used enzyme-linked immunosorbent assay (ELISA) to measure the level of LAMP5 in newly diagnosed MM patients, and the level was correlated to the clinical outcome of the patient.

Methods: A prospective study was done on 64 people, including 32 newly diagnosed MM patients and 32 age- and gender-matched healthy controls. ELISA was used to assess the levels of LAMP5 in serum samples. Clinical data and LAMP5 expression correlations were assessed.

Results: MM patients' LAMP5 levels were found to be statistically significantly higher than those of healthy controls (P<0.0001), However, LAMP5 does not correlate with clinical outcomes, laboratory results, or patient clinical data.

Conclusion: This report emphasizes that LAMP5 expression in newly diagnosed multiple myeloma patients was highly significant by ELISA and its influence on patient's prognosis still unclear as there was no significant correlation with other clinical data, which indicates more research on large scale of patients to determine its significance of its expression on prognosis.

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1. INTRODUCTION

The malignant plasma cell dyscrasia known as multiple myeloma is characterized by the bone marrow's clonal proliferation of plasma cells. Despite higher survival rates in the past decade due to the use of new drugs, therapy is not curative, and nearly all patients relapse (1).

LAMP-5 is a lysosome-associated membrane protein (LAMP) that is expressed in brain and plasmacytoid dendritic cells (pDC) in humans. PDCs, once stimulated, Toll-like receptor 9 (TLR9) is activated where LAMP-5 plays a role in its translocation from early endosomal to lysosomal signaling vesicle. Consequently, playing a role in controlling type 1 interferon (IFN-1) and pro-inflammatory cytokine release (2) Downregulation of LAMP5 resulted in enhanced IFN-1 signalling and decreased NF-kB signalling following stimulation of TLR9/interleukin 1(IL1) receptor. LAMP5 downregulation also resulted in a partial recovery of the cell growth inhibition upon depletion of Interferon Regulatory Factor 7 (IRF7). The expression of LAMP5 increased in MLL-leukemias and multiple myeloma, therefore targeting surface LAMP-5 leads to significant decrease the cell viability and improve the clinical outcome (3).

Our study used ELISA to assess the level of LAMP5 in newly diagnosed Multiple Myeloma patients and then correlated the level with clinical outcomes.

2. SUBJECTS AND METHODS

2.1. Participants

This prospective study was performed on 64 individuals divided into 32 newly diagnosed multiple myeloma patients recruited from Clinical Hematology Department and 32 healthy persons of matched sex and age in a period starting from November 2023 and May 2024.

All myeloma patients underwent a Complete history taking and general examination, the laboratory investigations included Complete blood count with differential (CBC), peripheral blood film, kidney function tests (serum creatinine), total proteins, albumin, serum protein electrophoresis (SPEP), immunofixation (IF), B2 microglobulin, serum Ca, albumin, total proteins, skeletal survey, echocardiography, bone marrow aspirate (BMA) for cytomorphology and flowcytometry to settle diagnosis. Patients were diagnosed by the international myeloma working group (IMWG) based on the presence of one or more of the following myeloma-defining events (MDEs): A bone marrow biopsy reveals 60% or more clonal plasma cells, a serum free light chain ratio of 100 or higher, and an absolute level of the implicated light chain of at least 100mg/L, More than one focal lesion on MRI that is at least 5mm or larger in size (4). All patients are classified initially for the staging according to The International Scoring System (ISS) (5,6). Patients started treatment and were Followed up by clinical assessment and investigations after 6 months after treatment.

All individuals provided written informed permission before participating in the study. This study received approval from the Faculty of Medicine, Ain Shams University Ethical Committee of Research, with number and date MS 623/2023 in concordance to the principles of the Declaration of Helsinki 1964.

2.2. Treatment protocol and response status

According to national comprehensive cancer network (NCCN) guidelines, triplet induction therapy was administered to all multiple myeloma patients who are eligible for a transplant (immunomodulatory agents, proteasome inhibitors, and dexamethasone). Bortezomib with lenalidomide and dexamethasone is the most used regimen (VRD) regimen, Although the combination of endoxan instead of lenalidomide also used in treatment of myeloma (VCD) regimen.

Conditioning with high dose melphalan 200mg/m2 and autologous stem cell transplantation is offered to all eligible patients (standard risk and high risk), as it is associated with superior disease-free survival compared with chemotherapy alone and is considered the preferred approach. Post-transplantation maintenance therapy with low-dose lenalidomide yields enhanced progression free survival (PFS) and overall survival (OS) (7).

The serologic remission states in Multiple Myeloma patients have been defined as Complete remission necessitates less than 5% bone marrow plasma cells and negative serum and urine immunofixation (IFE), VGPR is defined as 90% or more decrease in serum M protein and urine M-protein < 100 mg per 24 hours, or as serum and urine M protein detectable by IF but not on electrophoresis. A partial response occurs when a patient's blood monoclonal protein has decreased by more than 50% and M-protein in the urine has decreased by more than 90% (7).

3. METHODS

3.1. Measurement of serum level of lysosome-associated membrane protein (LAMP5)

Two ml of venous blood were obtained from each individual under perfect aseptic circumstances, deposited in a sterile vacutainer with a clot activator, and left to coagulate for 30

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minutes. Samples were centrifuged at 2000-3000 rpm for 20 minutes. The isolated serum was stored at (-80°C) to be used for the assay of LAMP5. Analysis of LAMP5 was done using quantitative enzyme-linked immune-sorbent assay (ELISA) kit provided by Bioassay Technology Laboratory, Nanhu dis, Zhejiang, China according to the manufacturer's instructions.

In order to detect the concentration of LAMP5 in the serum samples, a standard curve using linear scale was formed. The absorbance for each standard was plotted on the y-axis and the given concentrations of the standards were plotted on the x-axis. The best fit curve was obtained via the points on the graph. Zero standard absorbance was subtracted from all documented absorbances. The concentration of the samples was read directly from this standard curve by utilizing their optical density. The assay range (20 ng/L- 4200 ng/L). Sensitivity (15.625ng/L)

3.2. Statistical Analysis

Data were entered into the Statistical Package for Social Science (SPSS), categorized, edited, and saved (V.27.0, IBM Corp., USA, 2019). The quantitative data were reported as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data were found non-parametric. Similarly, qualitative variables were described as number and percentages. The following p-value was deemed significant: NS (non-significant), S (significant), and HS (highly significant) are denoted by P-values more than 0.05, less than 0.05, and less than 0.01 respectively. The Chi square test was used to examine the relation between two qualitative variables. To examine the significance between means of two groups, the student T test was used. The Mann-Whitney U test was used in non-parametric data to compare two independent groups. Correlation analysis using (Spearman's method) was performed to value the strength of association between two non-parametric Variables. The correlation coefficient expressed symbolically 'R' that identifies the strength (magnitude), and positive or negative to define the direction of the linear relationship between two variables. The ROC curve offers a useful means to estimate the sensitivity and specificity for quantitative diagnostic measures that classify cases into one of two groups.

4. RESULTS

Our study was conducted on 64 individuals who are comprised of 32 patients with newly diagnosed multiple myeloma and 32 sex and age matched apparently healthy individuals. The cases group were 21 females (65.6%) and 11 males (34.4%) with mean age 58.66±10.48 SD years while the controls were 11 males (34.4%) and 21 female (65.6%) with mean age 54.37 ± 10.58 years.

Demographic characteristics and laboratory data are showed in **Table 1**.

4.1. Comparison of patients and control groups regarding LAMP-5.

There was statistically significant rise in median LAMP5 level in cases group compared to controls group {9.12 ng/L (range 5.76 – 13.58) Vs 0.77 ng/L (range 0.49 – 1.07) , p-value <0.001}. According to the cut off value 9 ng/L , the patients were split into high expressers and low expressers, the percentage of patients with high expression (>9 ng/L) was significantly higher in patients than control group with p-value < 0.001 **(Table 2)**.

4.2. Correlation of LAMP5 with other studied parameters amongst the studied patients

There were no statistically significant correlations reported between LAMP5 level and the other studied parameters of the myeloma patients like (age, initial bone marrow aspirate, immunophenotyping and trephine, B2 microglobulin, serum protein electrophoresis, and others) as illustrated in **Table 3.**

4.3. Comparison of demographic and laboratory data comparing patients with low and high LAMP5 expression

There is no statistically significant correlation reported between high and low expressors of LAMP5 level regarding age, sex and laboratory parameters and osteolytic lesions, level of LDH, initial SPEP, initial IF, initial B2 microglobulin level, albumin level, ISS score, regimen, revaluation (MRD), SPEP level, IF and B2 studied parameters as shown in **Table 4.**

The best cut off point to differentiate between patients with multiple myeloma and control group by ROC curve was found to be > 1.96 with sensitivity of 100.0%, specificity of 96.87% and area under curve of 0.979 as illustrated in **Table 5, Figure 1.**

5. DISCUSSION

Multiple myeloma is a plasma cell cancer that is the second most prevalent hematological cancer which remains mostly incurable despite advances in treatments in the last decade **(4).** LAMP5 is a glycosylated protein and is one of the family of the LAMPS. In humans, LAMP5 is immersed in many

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Table 1. Myeloma patient demographics and laboratories data.

		Total No. = 32
Age	Mean ± SD	58.66 ± 10.48
Sex	Female Male	21 (65.6%) 11 (34.4%)
Initial BMA (plasma cell %)	Median (IQR) Range	45 (30 – 66.5) 10 – 95
Initial Trephine (plasma cell%)	Median (IQR) Range	53 (25 – 80) 0 – 90
Initial Serum Protein Electrophoresis (M spike)	Median (IQR) Range	1.63 (1.05 – 2.75) 0.7 – 9.7
Initial Serum calcium (mg/dl)	Mean ± SD Range	9.08 ± 1.18 5.7 – 11.9
Initial Hemoglobin level (gr/dl)	Mean ± SD Range	8.51 ± 1.19 6.4 – 11.5
Osteolytic lesions in skeletal survey	Absent Present	8 (25.0%) 24 (75.0%)
Initial (SPEP) (M band)	Mean ± SD Range	3.05 ± 1.90 0.2 – 9.7
Initial immunofixation (IF)	IgG kappa LC IgG kappa HC IgG kappa IgG lambda IgA kappa	16 (53.3%) 1 (3.3%) 9 (30.0%) 3 (10.0%) 1 (3.3%)
Initial B2 microglobulin	Mean ± SD Range	5.34 ± 2.47 2.5 – 13.9
Albumin(g/dl)	Mean ± SD Range	3.49 ± 0.50 2.4 – 4.5
Multiple Myeloma International Staging Score	Stage 1 Stage 2 Stage 3	8 (25.0%) 10 (31.2%) 14 (43.8%)
Chemotherapy Regimen	VCD VRD	18 (56.2%) 14 (43.8%)
Minimal residual disease (MRD) by flowcytometry	Median (IQR) Range	0.2 (0.04 – 1.15) 0 – 10
Remission Status	VGPR Refractory PR CR	15 (46.9%) 3 (9.4%) 11 (34.4%) 3 (9.4%)
Bone Marrow Transplantation	No Yes	31 (96.9%) 1 (3.1%)
Outcome	Alive	32 (100.0%)
Initial serum LAMP5 level by ELISA (ng/L)	Median (IQR) Range	9.12 (5.76 – 13.58) 2.43 – 25

VCD=velcade-cyclophosphamide-dexamethasone; VRD=velcade-revlimid dexamethasone; CR=complete remission; PR=partial remission; VRPR=very good partial remission.

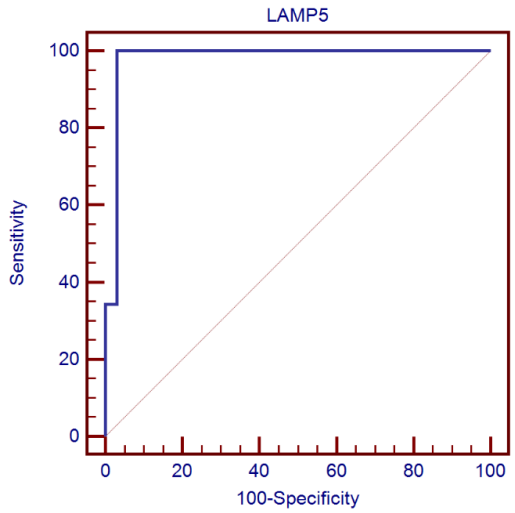

Figure 1. ROC curve to assess LAMP-5 to detect cases with multiple myeloma.

Table 2. Comparison of the LAMP-5 between the control and case groups.

		Control group	Cases group	Test value	P-value	Sig.
		No. = 32	No. = 32			
Serum LAMP5 level (ng/L)	Median (IQR)	0.77 (0.49 – 1.07)	9.12 (5.76 – 13.58)	-6.593	0.000	HS
	Range	0.29 – 11.45	2.43 – 25			
	Low expression (<9 ng/L)	31 (96.9%)	16 (50.0%)	18.023	0.000	HS
	High expression (>9 ng/L)	1 (3.1%)	16 (50.0%)			

Table 3. Correlation of LAMP5 with other studied parameters among the myeloma patients.

	LAMP5	
	R	P-value
Age	0.079	0.667
Initial BMA	0.010	0.956
Initial IPT	-0.170	0.351
Initial Trephine	-0.057	0.758
Initial Serum Creatinine Level	-0.112	0.541
Initial serum calcium	0.190	0.297
Initial Hemoglobin	-0.116	0.527
Initial Serum Protein Electrophoresis (M spike)	0.244	0.195
Initial B2 microglobulin	0.063	0.734
Albumin	-0.217	0.234
Minimal Residual Disease	-0.228	0.210
Follow up Serum Protein Electrophoresis	0.230	0.240
Follow up B2 microglobulin level	0.093	0.611

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Table 4. Comparison between patients with low LAMP5 expression and patients with high LAMP5 expression regarding demographic data and laboratory parameters.

		Low expression (<9) No. = 16	High expression (>9) No. = 16	Test value	P-value	Sig.
Age	Mean ± SD Range	57.56 ± 9.76 45 – 79	59.75 ± 11.37 35 – 79	-0.584	0.564	NS
Sex	Female Male	12 (75%) 4 (25%)	9 (56.3%) 7 (43.8%)	1.247	0.264	NS
Initial Bone Marrow Aspirate	Median (IQR) Range	42.5 (26.5 – 65) 10 – 90	50 (31 – 67.5) 10 – 95	-0.396	0.692	NS
Initial flowcytometry	Median (IQR) Range	34.5 (18 – 50) 2 – 87	29 (15 – 47.5) 10 – 88	-0.322	0.748	NS
Initial Trephine	Median (IQR) Range	53 (32.5 – 75) 8 – 90	52.5 (16.5 – 80) 0 – 90	-0.360	0.719	NS
Initial serum creatine level	Median (IQR) Range	1.95 (1.15 – 2.6) 0.8 – 9.3	1.35 (1 – 3) 0.7 – 9.7	-0.189	0.850	NS
Initial serum calcium level	Mean ± SD Range	8.98 ± 1.32 5.7 – 11.9	9.18 ± 1.06 7.5 – 10.9	-0.489	0.628	NS
Initial Hemoglobin level	Mean ± SD Range	8.66 ± 1.34 7 – 11.5	8.36 ± 1.03 6.4 – 9.8	0.710	0.483	NS
Osteolytic lesions	Absent Present	5 (31.3%) 11 (68.8%)	3 (18.8%) 13 (81.3%)	0.667	0.414	NS
Initial serum protein electrophoresis	Mean ± SD Range	2.77 ± 2.21 0.29 – 9.7	3.32 ± 1.56 0.2 – 6.4	-0.785	0.439	NS
Initial Immunofixation	IgG kappa LC IgG kappa HC IgG kappa IgG lambda IgA kappa	7 (46.7%) 1 (6.7%) 5 (33.3%) 1 (6.7%) 1 (6.7%)	9 (60%) 0 (0%) 4 (26.7%) 2 (13.3%) 0 (0%)	2.694	0.610	NS
Initial B2 microglobulin	Mean ± SD Range	5.39 ± 1.99 2.8 – 9.8	5.29 ± 2.95 2.5 – 13.9	0.106	0.917	NS
Albumin	Mean ± SD Range	3.61 ± 0.41 3.1 – 4.5	3.38 ± 0.57 2.4 – 4.3	1.350	0.187	NS
Multiple Myeloma International Staging Score	Stage 1 Stage 2 Stage 3	3 (18.8%) 6 (37.5%) 7 (43.8%)	5 (31.3%) 4 (25%) 7 (43.8%)	0.900	0.638	NS
Minimal Residual Disease (MRD)	Median (IQR) Range	0.5 (0.09 – 1.3) 0.01 – 3	0.15 (0.02 – 0.7) 0 – 10	-1.190	0.234	NS
Remission Status	VGPR Refractory PR CR	7 (43.8%) 1 (6.3%) 6 (37.5%) 2 (12.5%)	8 (50%) 2 (12.5%) 5 (31.3%) 1 (6.3%)	0.824	0.844	NS
Bone Marrow Transplant	No Yes	15 (93.8%) 1 (6.3%)	16 (100%) 0 (0%)	1.032	0.310	NS

Table 5. Receiver operating characteristic (ROC) curve to assess LAMP-5 to detect cases with multiple myeloma.

Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
>1.96	0.979	100.00	96.87	97.0	100.0

different properties of cell biology and can affect cellular processes and is playing a role in cancers (8,9). LAMP5 plays an important role in cancer progression. In stomach cancer, LAMP5 was elevated, and LAMP5 knockdown dramatically reduced cell invasion, migration, and proliferation while increasing apoptosis (10). In hematological malignancies it is highly expressed in MLL-leukemias and Multiple Myeloma cases and its reduction considerably slowed the proliferation of leukaemia cells (2 ,11). Our study measured the level of LAMP5 in newly diagnosed Multiple Myeloma cases and its correlation with the clinical outcome of the patients. The present research was a prospective cohort case-control study and embraced 32 patients newly diagnosed Multiple Myeloma in comparison to 32 control healthy subjects. To our best knowledge, this is first report of LAMP5 serology in the serum of newly diagnosed Multiple Myeloma patients.

Our research revealed a statistically significant distinction between the median level of LAMP5 in cases group compared to the healthy controls indicating that newly diagnosed Multiple Myeloma cases have significant expression of LAMP5 which matched with the study done by Chen and Ma who studied LAMP5 in patients with Multiple Myeloma using siRNA and found that patients with newly diagnosed multiple myeloma exhibit significant levels of LAMP5 expression and may involve in a crucial role in the occurrence and recurrence of MM (11).

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We could not find a correlation between LAMP5 overexpression and the initial proportion of plasma cells infiltrating bone marrow regarding aspirate, immunophenotyping and trephine. The initial percentage and type of the M band identified by immunofixation did not correlate with highly expressed LAMP5.

In our study there was no correlation between initial levels of serum calcium, serum creatinine, hemoglobin level, beta 2 microglobulin, osteolytic lesions which was in line with the results of Chen and Ma (11).

On the contrary to the results of Wang et al. study who found that high LAMP5 expression in newly diagnosed myeloma patients was significantly related with higher beta-2-microglobulin, high serum calcium, increased marrow infiltration by plasma cells. Additionally, a lower progression-free and overall survival rate was associated with higher LAMP5 expression. This controversy may be due to the technique used to detect LAMP5 which was done using myeloma cell line models. Flowcytometry was performed and LAMP5 was noticed on the surface of unpermeabilized LAMP5-positive myeloma cells (12).

Patients were split into two groups: those with high and low levels of LAMP5 expression according to the median of the IQR (9) for better assessment of the correlation between the overall highly expressed marker and the provided clinical data, and there was no correlation between the LAMP5 in both groups and the available clinical data which was similar to Chen and Ma study results that summarized that no significant correlation between high and low expression of LAMP5 and demographic and laboratory data of MM patients (10).

Also, the remission state and overall survival did not correlate with the highly expressed LAMP5. This was not in agreement with Chen and Ma who reported that patients with high LAMP5 expression had a poorer survival rate than those with low expression (11).

This can be attributed to the short duration of follow up. Further studies should be done on a large scale of patients associated with long period of follow up to detect the prognostic role of LAMP5 in multiple myeloma patients.

6. CONCLUSION

LAMP5 expression in newly diagnosed Multiple Myeloma patients was highly significant than control group using ELISA test and there was no significant correlation between its expression in those patients with disease prognosis.

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Conflict of interest

The authors declared no conflict of interest.

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Ethical statement

Not applicable.

References

1- Ledergor, G., Weiner, A., Zada, M. et al. (2018). Single cell dissection of plasma cell heterogeneity in symptomatic and asymptomatic myeloma. Nat Med 24, 1867–1876.

2- Gracia-Maldonado G, Clark J, Burwinkel M, et al ., (2022). LAMP-5 is an essential inflammatory-signaling regulator and novel immunotherapy target for mixed lineage leukemia-rearranged acute leukemia. Haematologica.; 107(4):803-815.

3- Gracia-Maldonado, G., Clark, J., Pierre, P., et al ., (2018). The Role of LAMP5 in Innate Immune Signaling Is Critical for the Survival of MLL Leukemias. Blood, 132, 3900.

4- Rajkumar, S., Dimopoulos, M., Palumbo, A. (2014). International Myeloma Working Group Updated Criteria for the Diagnosis of Multiple Myeloma. The Lancet Oncology, 15(12), e538-548.

5- Palumbo A, Avet-Loiseau H, Oliva S, Lokhorst HM, et al., (2015). Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group. J Clin Oncol. 10;33(26):2863-9.

6- Martin W. Schoen, Suhong Luo, Brian Gage, Kenneth Robert Carson, Kristen Marie Sanfilippo, (2018). Journal of Clinical Oncology, 36:15_suppl, 8051-8051.

7- Harousseau, J. L., Attal, M., & Avet-Loiseau, H.et al ., (2009). The role of complete response in multiple myeloma. Blood, The Journal of the American Society of Hematology, 114(15), 3139-3146

8- de Larrea C. F., Tovar N., Rozman M et al ., (2011). Multiple myeloma in serologic complete remission after autologous stem cell transplantation: impact of bone marrow plasma cell assessment by conventional morphology on disease progression. Biology of blood transplantation, 17(7), 1084-1087.

9- Harousseau, J. L., Attal, M., & Avet-Loiseau, H.et al ., (2009). The role of complete response in multiple myeloma. Blood, The Journal of the American Society of Hematology, 114(15), 3139-3146.

10- Umeda S, Kanda M, Shimizu D, et al., (2022). Lysosomal associated Membrane Protein Family Member 5 Promotes the Metastatic Potential of Gastric Cancer Cells. Gastric Cancer; 25(3):558–72.

11- Chen, Y., & Ma, T. (2023). LAMP5 may promote MM progression by activating p38. Pathology and Oncology Research, 29, 1611083.

12- Wang, H., Rueda, L. Y. M., Dang, M., Lee, et al ., (2023). Lysosomal Associated Membrane Protein Family Member 5 (LAMP5) As a Novel Mediator of, and Target in High Risk Multiple Myeloma (MM). Blood, 142, 873.

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