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Platelet-derived growth factor levels in Iraqi multiple myeloma patients: a case-control study

Ghazi Mohamad Ramadan[1,2], Hafidh I. Al-Sadi[3], Saja I. Alkafaji[4], Hayder Abdul-Amir Makki Al-Hindy[5,*], Mazin Jaafar Mousa[6], Heba S. Jawad[7], Shahlaa Kh. Chabuk[8], Rana J. Abbas[9], Metab Hasan Abd Ali[10], Mina Mohammed Makki[10], Fatima Hussein Hadi[10], Noor Alhuda Tahreer Dawood[10]

[1]Syrian Fertility Center, Tartus, Syria
[2]Department of Anaesthesia and Intensive Care, Al-Taff University College, Karbala, Iraq
[3]College of Pharmacy, University of Mashreq, Baghdad, Iraq
[4]Department of Medical Laboratory Techniques, College of Health and Medical Techniques, Al-Mustaqbal University, Hillah, Iraq
[5]Department of Pharmacology and Toxicology, College of Pharmacy, University of Babylon, Hillah, Iraq
[6]Department of Clinical Laboratories, College of Pharmacy, University of Babylon, Hillah, Iraq
[7]College of Education for Pure Science, Al-Zahraa University for Women, Karbala, Iraq
[8]Department of Physiology, Hammurabi College of Medicine, University of Babylon, Hillah, Iraq
[9]Department of Radiological Techniques, College of Health and Medical Techniques, Al-Zahraa University for Women, Karbala, Iraq
[10]College of Pharmacy, University of Babylon, Hillah, Iraq

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*** CORRESPONDING AUTHOR:**
Hayder Abdul-Amir Makki Al-Hindy, Department of Pharmacology and Toxicology, College of Pharmacy, University of Babylon, Hillah, Iraq; e-mail: phar.hayder.abdul@uobabylon.edu.iq

ABSTRACT

Multiple myeloma (MM), the second most prevalent haematological malignancy, is characterized by monoclonal plasmacytosis within the bone marrow. Platelet-derived growth factor (PDGF), a key mediator of angiogenesis and tumorigenesis, has been implicated in the pathophysiology of MM. This study aimed at investigating whether pre-treatment serum levels of PDGF correlate with MM diagnosis, disease stage, and therapeutic response. A case-control study was conducted involving 55 Iraqi patients diagnosed with MM and 25 healthy controls. Participants were recruited from the Department of Haematology at the Marjan Medical Hospital, Babil Province, Iraq, between March 2021 and December 2022. Serum PDGF concentrations were quantified using enzyme-linked immunosorbent assay (ELISA). MM patients exhibited higher mean PDGF levels than controls (mean difference: 187.3 pg/mL), although this difference did not reach statistical significance (p=0.077). Among MM patients, those receiv-

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ing treatment demonstrated significantly lower platelet counts (p=0.012) and elevated serum urea levels (p=0.045) compared to untreated counterparts. Receiver operating characteristic (ROC) curve analysis revealed poor diagnostic accuracy of PDGF for MM (area-under-the-curve; AUC: 0.575; p=0.030), as well as limited discriminatory power between stage II and stage III disease (AUC: 0.586; p=0.059). In conclusion, although serum PDGF levels alone do not constitute a statistically significant or specific diagnostic biomarker for MM, the findings underscore the need for further investigation into the combined utility of PDGF and other molecular markers to improve diagnostic and prognostic stratification in MM.

1. Introduction

Plasma cell myeloma (multiple myeloma; MM) is a malignancy characterized by the uncontrolled proliferation of plasma cells within the bone marrow, with an incidence rate of 4.5–6 per 100,000 individuals[1]. It ranks second only to non-Hodgkin lymphoma among common haematological neoplasms. MM arises from dysregulated bone remodelling, wherein bone formation is diminished relative to accelerated bone resorption. Diagnostic criteria for MM include the detection of monoclonal proteins (M-proteins) in plasma or urine. Although MM remains incurable, recent therapeutic advances have significantly improved patient outcomes[2].

Myeloproliferative disorders, including MM, are marked by pathological angiogenesis. It is hypothesized that imbalances between pro-angiogenic and anti-angiogenic factors influence tumor perfusion and progression[3]. Several cytokines with tumorigenic potential – such as the fibroblast growth factor-2[2], the vascular endothelial growth factor[4], and the platelet-derived growth factor (PDGF) – have been implicated in MM. PDGF, in particular, regulates key cellular functions in MM, including proliferation and migration. Consequently, PDGF is considered a candidate biomarker for MM diagnosis and staging. This study aims to evaluate the clinical relevance of serum PDGF levels and to determine their association with MM diagnosis, disease stage, and comparison to healthy controls.

2. Methodology

A case-control study was conducted at the Oncology Center of Merjan Medical City, Babylon, Iraq. The study included 55 patients diagnosed with MM and 25 healthy volunteers aged 38–72 years. Patient recruitment occurred at the Department of Haematology of the Marjan Medical Hospital, Babil Province, Iraq, from March 2021 to December 2022. MM diagnoses were confirmed by specialist haematologists. Control subjects were age-matched and free from acute or chronic illnesses.

Patients were undergoing first-line cytotoxic chemotherapy with either lenalidomide or bortezomib. They were stratified into four groups: group I comprised 26 patients with stage II MM; group II included 16 patients with stage III MM; group III consisted of 6 newly diagnosed stage II patients; and group IV included 7 newly diagnosed stage III patients. Groups III and IV were classified as untreated for analytical purposes.

Exclusion criteria included type 1 diabetes mellitus, renal or hepatic failure, prior bone marrow transplantation, and use of alternative MM therapies. Venous blood samples (5 mL) were collected from each participant for biochemical analysis. Socio-demographic data and haematological / biochemical test results were extracted from the patients' records.

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Table 1. Diagnostic potential of serum and clinical markers in differentiating stages of multiple myeloma (MM). Abbreviations used: AUC, area-under-the-curve; CI, confidence interval; PDGF, platelet-derived growth factor; ROC, receiver operating characteristic.

			ROC analysis			
Variable	**Group comparison**	***p*-value**	**AUC**	**Specificity, sensitivity**	**95% CI**	***p*-value**
Age (years)	Control *vs* MM Patients	0.088	0.575	0.625, 0.56	0.485–0.665	0.03
Platelets (×10^3)	Control *vs* MM Patients	0.001	0.575	0.625, 0.56	0.485–0.665	0.03
Blood urea (mg/dL)	Control *vs* MM Patients	0.059	0.575	0.625, 0.56	0.485–0.665	0.03
Serum creatinine (mg/dL)	Control *vs* MM Patients	0.082	0.575	0.625, 0.56	0.485–0.665	0.03
Serum PDGF (pg/mL)	Control *vs* MM Patients	0.077	0.575	0.625, 0.56	0.444–0.707	0.03
Age (years)	Stage II *vs* Stage III MM	0.061	0.586	0.619, 0.67	0.480–0.692	0.059
Platelets (×10^3)	Stage II *vs* Stage III MM	0.012	0.600	0.650, 0.68	0.490–0.710	0.050
Blood urea (mg/dL)	Stage II *vs* Stage III MM	0.045	0.590	0.630, 0.66	0.475–0.705	0.047
Serum creatinine (mg/dL)	Stage II *vs* Stage III MM	0.092	0.570	0.600, 0.65	0.465–0.675	0.089
Serum PDGF (pg/mL)	Stage II *vs* Stage III MM	0.059	0.586	0.619, 0.67	0.480–0.692	0.059

Serum PDGF concentrations were measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) kit (Elabscience®) at the College of Pharmacy research laboratory. Data were analysed using the Statistical Package for the Social Sciences (SPSS, IBM). Receiver operating characteristic (ROC) curve analysis and logistic regression were employed in order to calculate the area-under-the-curve (AUC), sensitivity, and specificity for combined biomarkers. Cross-validation was performed in order to ensure analytical robustness, with statistical significance set at $p<0.05$.

Ethical approval was granted by local health authorities and the Institutional Review Board (IRB) of the College of Pharmacy, University of Babylon (IRB number: A0032; date: 1-2022). Informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

3. Results and Discussion

Age demonstrated limited discriminative capacity between MM stages, with an AUC of 0.586 ($p=0.059$), indicating no statistically significant difference. Among all evaluated parameters, platelet count exhibited the highest diagnostic accuracy (AUC: 0.600, specificity: 0.650, sensitivity: 0.680; $p=0.012$). Blood urea levels also showed reasonable diagnostic utility (AUC: 0.590; $p=0.045$), while serum creatinine was less effective in stage differentiation (AUC: 0.570; $p=0.092$). Serum PDGF yielded a moderate AUC of 0.586 ($p=0.059$), suggesting limited standalone diagnostic value (Table 1).

Although MM patients exhibited elevated serum PDGF levels compared to healthy individuals, the difference was not statistically significant. PDGF also demonstrated poor performance in distinguishing between stage II and stage III MM. The role of angiogenesis in tumor pathogenesis is well established[2], and PDGF is recognized as a key mediator in this process. Previous studies have explored PDGF receptor expression in MM and reported associations with disease prognosis[2,5]. However, the immunological implications of monoclonal immunoglobulin gammopathy in MM remain uncertain, particularly regarding cytokine-mediated modulation of myeloma cell intermediates[1].

PDGF is known to enhance endothelial cell migration and has recently been identified as a major cytokine involved in MM pathogenesis, affecting

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both neoplastic and normal cellular environments[6]. Contrasting findings from other studies suggest that elevated PDGF receptor expression correlates with advanced disease stages[7], while others report reduced plasma PDGF-BB levels in MM patients relative to healthy controls[8].

Platelets are implicated in tumor growth, invasion, and chemoresistance[2]. The heightened platelet reactivity observed in MM may have confounded PDGF measurements, as MM patients in this study exhibited significant differences in platelet counts compared to controls.

Although patients were not stratified by specific chemotherapeutic agents, all received treatment at a single center to minimize confounding variables. Existing literature indicates that PDGF contributes to the stabilization of stressed microvascular phenotypes via pericytes and vascular smooth muscle cells[5,8]. Some researchers propose that PDGF-β may function as a latent angiogenic factor in haematological malignancies, with microvascular density positively correlating with MM progression[1,5,8].

Despite the absence of treatment-based stratification, uniform therapeutic protocols were applied to all participants to reduce bias. The observed discrepancies in PDGF levels before and after chemotherapy suggest that PDGF may serve as a marker of immune status in advanced MM. PDGF appears to play a multifaceted role in cancer biology, acting as an antitumor factor in tumours with high PDGF production, and as a potent growth factor in those with lower expression.

The age distribution of MM patients in this study aligns with trends reported in other populations, indicating broad demographic representation. Ongoing research continues to identify molecular mechanisms and therapeutic targets that drive MM progression, underscoring the need for novel treatment strategies[2]. This study does not advocate for PDGF as a definitive biomarker; rather, it highlights the potential of molecular genetic analyses to elucidate PDGF-related oncogenic pathways and inform drug development targeting MM-specific PDGF signalling. Further research is warranted in order to clarify the functional role of PDGF in malignancy and to enhance therapeutic precision.

4. Conclusion

Serum PDGF demonstrates limited diagnostic utility in distinguishing stage II from stage III MM. Although PDGF is involved in angiogenesis and tumor progression, its low sensitivity precludes its use as a standalone biomarker. Platelet count and blood urea levels showed stronger staging performance, with statistically significant *p*-values, whereas age and serum creatinine were only moderately predictive. These findings support the need for multi-marker approaches so as to improve MM diagnostic accuracy and refine staging and treatment strategies.

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Conflicts of interest

None exist.

ORCIDs

0000-0002-5266-0233 (G.M. Ramadan); 0000-0001-5794-2603 (H.I. Al-Sadi); 0009-0009-8332-9373 (S.I. Alkafaji); 0000-0001-6232-8501 (H.A.A.M. Al-Hindy); 0000-0003-2209-010X (M.J. Mousa); 0000-0002-6231-4393 (H.S. Jawad); 0000-0003-1254-0437 (S.K. Chabuk); 0000-0002-6136-6837 (R.J. Abbas), 0009-0003-8068-9927 (M.H. Abd Ali); 0009-0003-5701-362X (M.M. Makki); 0009-0005-5304-2364 (F.H. Hadi); 0009-0007-2671-3470 (N.A.T. Dawood)

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