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The role of Monocyte Chemoattractant Protein -1 (MCPI) as a predictor of outcome in polytraumatized patients

MJ Balogun[1], TO Alonge[2], SO Ogunlade[2] and T Ogunleye[3]

Department of Orthopaedics and Trauma[1], University College Hospital, Department of Surgery[2], College of Medicine, University of Ibadan and Department of Chemical Pathology[3], University College Hospital, Ibadan, Nigeria.

Abstract

Background: Trauma has been tagged a modern international epidemic and the commonest causes of mortality following polytrauma include severe infections leading to multiple organ dysfunction syndrome or multiple organ failure.

Materials and methods: Patients with polytrauma admitted through the Accident and Emergency department (now simply referred to as the Emergency Department) that satisfy the defined criteria were recruited and had their blood samples taken into an endotoxin free EDTA bottles at 48 ± 2 hours after trauma and samples stored at -80^0 Celsius until analyzed. Serum MCP-1 level was estimated for each patient using the Human MCP-1 ELISA kit based on the manufacturer's guide. In addition, the Revised Trauma Score comprising of the Glasgow Coma Scale Score, Respiratory Rate and Systolic Blood Pressure at presentation was documented for each patient.

Results: 110 polytrauma patients had their sera assayed for MCP-1. The patient's ages ranged from 18 to 80 years. The mean age was 39.98 ± 14.369 years; 2.7% of patients were less than 20 years, 23.6% were aged between 20 and 29years, 27.3% were aged between 30 and 39years, 24.5% were aged between 40 and 49years, 9.1% were aged between 50 and 59years whilst 12.7% were above 60years. Majority (27.3%) of the patients were in the age group of 30-39 years. The MCP-1 values ranged from 10 to 2,841, while that of Revised Trauma Score ranged from 5 to 12. The mean MCP-1 level and Revised Trauma Score were 284.018 ± 454.074 and 11.245 ± 1.491 respectively. There was no significant correlation between MCP-1 level and Revised Trauma Score (r =-0.123, p =0.200).

Conclusion: There is no correlation between serum levels of Monocyte Chemoattractant Protein-1(MCP-1) and the severity of injury in polytrauma patients as assessed by the Revised Trauma Score and thus serum MCP-1 values may not be an appropriate marker in predicting outcome.

Keywords: *Monocyte Chemoattractant Protein -1, Polytrauma, Revise trauma score*

Correspondence: Dr. M.J. Balogun, Department of Orthopaedics and Trauma, University College Hospital, Ibadan, Nigeria. E-mail: mosibalogun@gmail.

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Introduction

Trauma is a major health problem all over the world, leading to death and disability especially in the first three decades of life [1]. With the advent of technology and sophistication in high speed travel, road traffic crashes still dominate as the causal mechanism for trauma related deaths [2]. Polytrauma, defined as injuries affecting at least two different organ systems or organs, with at least one of them being life threatening [4] accounts for approximately 16-18% of all trauma globally and it has a mortality rate of 15-50% [3].

Trauma as a disease entity is now referred to as a modern international epidemic and the commonest causes of mortality following polytrauma include severe infections which ultimately lead to multiple organ dysfunction syndrome or multiple organ failure [5]. Trauma fulfills the disease classification criteria for a global pandemic and its' occurrences and significance as a cause of morbidity and mortality cuts across continents, despite efforts toward its prevention worldwide.

Monocyte Chemoattractant Protein-1(MCP-1), a member of the C-C Chemokine family and also referred to as C-C Chemokine Ligand 2 (CCL2), Monocyte Chemotactic and Activating factor, Monocyte Secretory Protein CCL2, is a potent chemotactic factor for monocytes [6]. The structure of MCP-1 was first identified in 1997 and it was classified into 4 subfamilies on the basis of the number and location of the cysteine residue at the N-terminus of the molecule and are named CXC, C-C, CX_3C and C in agreement with the systematic nomenclature [7].

In wild type control mice, mRNA transcription of macrophage inflammatory protein (MIP)-1á, MIP-1â2 and MCP-1 as well as their major receptor CCR5 and CCR2 respectively increases after freeze injury and gradually returns to control pre-injury levels by 14 days' post injury. In animal experiments, high levels of MCP-1 mRNA have been found in the brain 6 hours after cerebral ischemia. The maximal expression of this chemokine was observed between 12 hours and 48 hours post injury. [8,9].

Shear stress has been shown to mediate a biphasic response to MCP-1 gene expression in vascular endothelial cell. The MCP-1 gene expression decrease to basal level at 4 hours and then decline further to become quiescent at 5 hours after the onset of shear stress [10].

Following significant trauma, macrophages are attracted by several chemokines which initiate immunological defense and repair [7,11]. MCP-1 is a major attractant for macrophages and monocytes but not neutrophils, and the mechanism by which MCP-1 mediates neutrophil infiltration is not clear [7,12,13]. Monocytes which becomes macrophages after emigrating from the blood stream inhabiting various tissues comprise the mononuclear phagocyte system [14,15] . Studies have shown that monocyte chemoattractant protein-1 is up-regulated under stressful conditions such as polytrauma particularly those associated with significant haemorrhage via its receptor CCR2 [11].

Several injury severity scales exist in clinical practice however, the Revised Trauma Score (RTS) is the most widely used physiologic measure and it is a reliable tool for assessing the severity of most traumatic injuries [16]. The Revised Trauma Score is derived from neurological assessment using the Glasgow Coma Scale Score along with two physiological parameters: Respiratory Rate and Systolic Blood Pressure. Glasgow Coma Scale score estimated after resuscitation of patient is noted to be the best for the assessment of Injury Severity. These indices are scored between zero (worst status) and 4 (best status). Despite its drawback, RTS is reputed to fairly correlate well with the chances of mortality from polytrauma [16,17]

Polytrauma is rife in our environment and there is paucity of knowledge about the correlation between Monocyte Chemoattractant Protein-1 and Injury Severity using the Revised Trauma Score. The aim of this research is to seek to unravel any correlation between serum levels of the chemokine Monocyte Chemoattractant Protein-1 secreted in polytrauma and injury severity as assessed by the Revised Trauma Score and to ascertain whether the MCP-1 values could be used to prognosticate or predict clinical outcome. Ethical approval was obtained from the University of Ibadan/University College Hospital Ethical Review Committee

Patients and methods

This hospital based prospective study of polytrauma patients presenting at the emergency department of the University College Hospital, Ibadan was carried out within a period of twelve [12] months between February 2016 and January 2017. Patients, aged 18 years and above with polytrauma, that presented to the Emergency department alive for treatment were recruited into this study whilst patients aged less than 18 years of age, die within 48 hours of presentation, or had initial care in another hospital were excluded.

The Glasgow Coma Scale Score was estimated after resuscitation, the Respiratory Rate and the Systolic Blood Pressures were recorded into a proforma. Venous peripheral blood was drawn from each polytrauma patient at 48 ± 2 hours post injury into a pyrogen/endotoxin free Potassium Ethylenediamine Tetra-acetic Acid (EDTA) coated bottles and centrifuged and the plasma immediately refrigerated at -80^{o}C until ready for estimation of the plasma levels of MCP-1, using commercially available human ELISA kit, according to the manufacturer's instruction. Informed consent were obtained from the patents or their next-of-kin before the blood samples were obtained and the data obtained were coded and analyzed using SPSS Version 20.0

Descriptive statistics of frequency count and percentages were carried out. Averages, standard deviation, minimum and maximum values were obtained. Inferential statistics of Student t-test, Pearson moment correlation were applied at 5% level of significance

Results

A total of 114 patients were recruited into the study, however, only 110 patients whose samples were adjudged adequate were assayed for MCP-1; giving a response rate of approximately 96.5%. Their data are as shown below.

Table 1: Socio-demographic characteristics.

Socio-demographic characteristics (n=110)	Frequency	Percentage (%)
Patients Age (years)		
<20	3	2.70
20-29	26	23.60
30-39	30	27.30
40-49	27	24.50
50-59	10	9.10
≥60	14	12.70
Mean (SD)	39.98 ± 14.37 years	
Range	18 to 80 years	
Outcome		
Discharged	101	91.80
Dead	9	8.20
Total	110	100.00

The patient's age ranges from 18 to 80 years. The mean age was 39.98 ± 14.37 years: 2.7% [3] of the patients were less than 20 years, 23.6% [26] were between 20-29 years, 27.3%(30) were between 30-39 years, 24.5% [27] were between 40-49years, 9.1% [10] were between 50-59years, 12.7% [14] were aged greater than 60 years. Majority 30 (27.3%) of the patients were in the 30-39-year age group

The patient with the highest combination of injury had injuries to the Head and Neck, Face, Chest, Abdomen, Extremity fractures and Skin with a mean MCP-1 value of 463 as shown above.

There is no significant correlation between MCP-1 level and Revised Trauma Score (r =-0.123, p=0.200). The MCP-1 level ranges from 10 to 2841, while that of Revised Trauma Score ranges from 5 to 12. The mean MCP-1 level and Revised Trauma Score were 284.018 ± 454.074 and 11.245 ± 1.491 respectively as shown in Table 4 above.

Table 2: The combined pattern of injury with MCP-1

Combined pattern of injury	N	Mean	Std. dev.	Min	Max
A,PC,S	1	78	78	78	78
C,A	2	154	15.56	143	165
C,A,EF	1	416	416	416	416
C,A,S	1	83	83	83	83
C,EF	2	78.0	12.73	69	87
C,EF,S	2	118	9.89	111	125
EF,S	18	427.61	685.89	22	2687
F,C,EF,PG	1	132	132	132	132
F,EF,S	1	214	214	214	214
F,S	1	21	21	21	21
HN,A,EF	1	137	137	137	137
HN,A,PC	1	265	265	265	265
HN,C	1	124	124	124	124
HN,C,EF	2	316	387.49	42	590
HN,EF	10	199.40	220.57	41	781
HN,EF,PG	1	189	189	189	189
HN,EF,PG,S	1	109	109	109	109
HN,EF,S	23	283.17	384.60	28	1664
HN,F	1	45	45	45	45
HN,F,C,A,EF,S	1	463	463	463	463
HN,F,C,S	1	131	131	131	131
HN,F,EF	3	168	92.86	101	274
HN,F,EF,S	2	506.50	382.54	236	777
HN,F,S	6	189.17	270.56	18	734
HN,PC,S	1	269	269	269	269
HN,PG,S	1	947	947	947	947
HN,S	22	273.18	618.06	10	2841
PC,EF	2	710.50	258.09	528	893

Key to the abbreviations: A – Abdominal Injury, C – Chest Injury, EF – Extremity fracture, F – Facial Injury, HN – Head & Neck Injury, PC – Pelvic content, PG – Pelvic girdle, S – Skin laceration

Discussion

Trauma remains the most common cause of death in people under the age of 44 years worldwide [18]. Our study showed the vulnerability of those below the age of 40 years and also the male sex preponderance to trauma and this is in keeping with other studies on trauma in our region and globally

Table 3: Correlation between MCP-1 level and Revised Trauma Score in polytrauma patients.

Variables	N	Mean	Standard deviation	Correlation (r) value	Minimum	Maximum	p-value	Remark
MCP-1 Level	110	284.01	454.07	-0.123	10	2841	0.200	Not Significant
Revised Trauma Score	110	11.24	1.49		5	12		

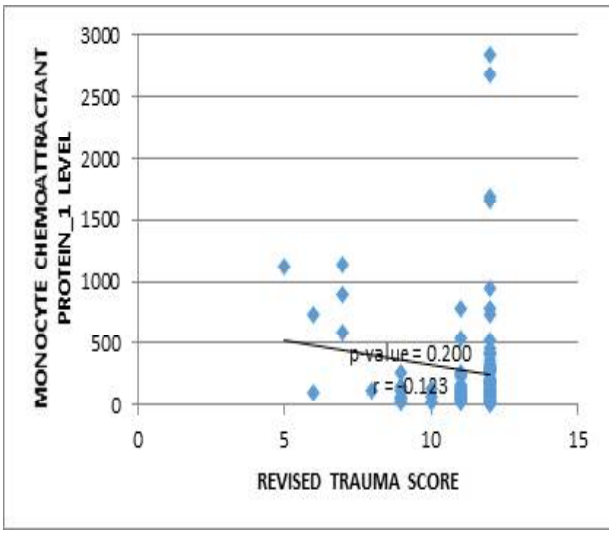

Fig.1: This scatter plot shows the relationship between MCP-1 level and Revised Trauma Score in polytrauma patients.

[19]. Economic and social activities often involve young male individuals who are mostly the breadwinners [19, 20] and majority of the patients (75.3%) were in the age group of 20-49 years and this finding is similar to various reports in literature. Following admission, the patients were followed up on the wards and the outcome of patients in our study showed that 91.8% of patients were discharged after variable number of days, whilst 8.2% died during the course of admission. This is comparable to a study in Sokoto, North Western Nigeria by Oboirien *et al* in which they found the mortality rate to be 9.5% and those with major disability at 9.5% whilst those with minor disability accounted for 7.1% [19] of their study on polytrauma.

Recently, accumulating evidences demonstrated that MCP-1 genetic variations within the regulatory regions could make patients susceptible to certain inflammation-related diseases, infection and sepsis by altering MCP-1 expression levels [21,22] . MCP-1 has been shown to correlate with severity of trauma and pro-inflammatory cytokine IL-6 though and Wang *et al* demonstrated that plasma MCP-1 levels were significantly increased in patients with severe trauma, and that early plasma MCP-1 was significantly correlated with injury severity and the risk of developing sepsis in severe trauma patients [23] .

However, in our study, values of MCP-1 did not seem to increase in consonant with increasing injury severity as depicted by increasing values of revised trauma score.

Limitation

The work is limited principally by scarcity of published clinical data regarding MCP-1 and polytrauma. Values of MCP-1 may have been altered in patients who were clinically unstable thereby warranting various forms of resuscitation and the cost of procuring the MCP-1 Elisa Kit in a poor resource setting is substantial.

Conclusion

There is no correlation between Monocyte Chemoattractant Protein-1 and the severity of injury in polytraumatized patients as assessed by the Revised Trauma Score, and this chemokine (MCP-1) may not be a predictive maker of injury severity or predict outcome in polytrauma.

References

1. Krug EG, Sharma GK and Lozano R. The Global Burden of Injuries. 2000; 90(4):4.
2. Solagberu BA and Adekanye AO, ofoegbu CPK, Udoffa US. Epidemiology of Trauma Deaths. WAJM. 2003 Jun;22:2.
3. Acosta JA, Yang JC, Winchell RJ, Simons RK and Fortlage DA, Hollingsworth-Fridlund P, et al. Lethal Injuries and Time to Death in a Level I Trauma Center. J Am Coll Surg. :6.
4. Polytrauma with injuries to the musculo-skeletal system, clinical and therapeutical aspects.pdf [Internet]. [cited 2020 Aug 3]. Available from:

http://www.umfcv.ro/files/p/o/Polytrauma%20with%2 0injuries%20to%20the%20musculo-skeletal%20system,%20clinical%20and%20therapeutical% 20aspects .pdf

5. Gwaram U, Ihezue C and Onche I. Assessing the severity of injury using the revised trauma score in a tertiary institution in North-Central Nigeria. Niger J Basic Clin Sci. 2013;10(1):3.
6. Lecky FE, Bouamra O, Woodford M, Alexandrescu R and O'Brien SJ. Epidemiology of Polytrauma. In: Pape H-C, Peitzman A, Schwab CW, Giannoudis PV, editors. Damage Control Management in the Polytrauma Patient [Internet]. New York, NY: Springer New York; 2010 [cited 2020 Jul 20]. p. 13–24. Available from: http://link.springer.com/10.1007/978-0-387-89508-6_2
7. Cochran BH, Reffel AC and Stiles CD. Molecular Cloning of Gene Sequences Regulated by Platelets-derived Growth Factors. 1983 Jul;33:939–947.
8. Shelley O, Murphy T, Paterson H, Mannick JA and Lederer JA. Interaction Between the Innate and Adaptive Immune Systems is Required to Survive Sepsis and Control Inflammation After Injury: Shock. 2003 Aug;20(2):123–129.
9. Yamagami S, Tamura M, Hayashi M, *et al*. Differential production of MCP-1 and cytokine-induced neutrophil chemoattractant in the ischemic brain after transient focal ischemia in rats. J Leukoc Biol. 1999 Jun;65(6):744–749.
10. Wang X, Yue T-L, Barone FC and Feuerstein GZ. Monocyte Chemoattractant Protein–1 Messenger RNA Expression in Rat Ischemic Cortex. Stroke. 1995 Apr;26(4):661–666.
11. Shyy YJ, Hsieh HJ, Usami S and Chien S. Fluid shear stress induces a biphasic response of human monocyte chemotactic protein 1 gene expression in vascular endothelium. Proceedings of the National Academy of Sciences. 1994 May 24;91(11):4678–4682.
12. García-Ramallo E, Marques T, Prats N, *et al*. Resident Cell Chemokine Expression Serves as the Major Mechanism for Leukocyte Recruitment During Local Inflammation. J Immunol. 2002 Dec 1;169(11):6467–6473.
14. Hildebrand F, Hubbard WJ, Choudhry MA, *et al*. Kupffer Cells and Their Mediators. The American Journal of Pathology. 2006 Sep;169(3):784–794.
15. Frink M, Lu A, Thobe BM, *et al*. Monocyte chemoattractant protein-1 influences trauma-hemorrhage-induced distal organ damage via regulation of keratinocyte-derived chemokine production. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2007 Mar;292(3):R1110–6.
16. Engelhardt E, Toksoy A, Goebeler M, *et al*. Chemokines IL-8, GROá, MCP-1, IP-10, and Mig Are Sequentially and Differentially Expressed During Phase-Specific Infiltration of Leukocyte Subsets in Human Wound Healing. The American Journal of Pathology. 1998 Dec;153(6):1849–1860.
17. Dd T. Trauma. Accidental and intentional injuries account for more years of life lost in the U.S. than cancer and heart disease. Among the prescribed remedies are improved preventive efforts, speedier surgery and further research [Internet]. Vol. 249, Scientific American. Sci Am; 1983 [cited 2020 Sep 11]. Available from: https://pubmed.ncbi.nlm.nih.gov/6623052/
18. El Mestoui Z, Jalalzadeh H, Giannakopoulos GF and Zuidema WP. Incidence and etiology of mortality in polytrauma patients in a Dutch level I trauma center: European Journal of Emergency Medicine. 2017 Feb;24(1):49–54.
19. M O and S U. The Conundrum of Polytrauma in Sokoto, North-West Nigeria. J Trauma Treat [Internet]. 2016 [cited 2020 Jul 30];5(2). Available from: http://www.omicsgroup.org/journals/the-conundrum-of-polytrauma-in-sokoto-northwest-nigeria-2167-1222-1000301.php?aid=71642
20. He J, Chen Y, Lin Y, *et al*. Association study of MCP-1 promoter polymorphisms with the susceptibility and progression of sepsis. PLOS ONE. 2017 May 4;12(5):e0176781.
21. Sambyal V, Guleria K, Kapahi R, Manjari M and Sudan M. Association of the -2518 A/G Polymorphism of MCP with Breast Cancer in punjab, North-West India. Asian Pacific Journal of Cancer Prevention. 2015;16:743–7.
22. Gl S, L Y, Y S, Yj Y and Cx S. MCP-1 gene polymorphisms in North Chinese patients with pulmonary tuberculosis. Genet Mol Res. 2015 Apr 27;14(2):4035–40.
23. Wang Y, Liu Q, Liu T, *et al*. Early plasma monocyte chemoattractant protein 1 predicts the development of sepsis in trauma patients. 2018;6.

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