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Serum levels of monocyte chemoattractant protein-1 has no correlation with gender and age in polytrauma

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ABSTRACT

Background: Trauma is one of the commonest causes of death among young people with significant increase in morbidity and mortality. Following injuries to tissues, the body responds in an attempt to cause repair of the damaged tissue. Although its significance depends on the interplay of various factors involving neurohormonal and immune responses. Monocyte chemoattractant protein-1 (MCP-1) is a pro-inflammatory chemoattractant produced by the monocyte and causes the further release of chemokines and cytokines needed at the site of tissue injury. It therefore plays a critical role in tissue healing.
Methods: This was a prospective hospital-based study carried out at University College Hospital (UCH), Ibadan. Polytrauma patients admitted through the accident and emergency department that met a defined criteria were recruited and had their blood samples taken into an endotoxin free test tube at 48±2 hours after trauma. MCP-1 levels in the serum were estimated though the human MCP-1 enzyme-linked immunosorbent assay (ELISA) kit. This process was carried out using the ELISA technique based on the producer's guide.
Results: 110 patients were recruited for the study. There was no significant difference in gender variations in MCP-1 level (t=-0.935, p=0.351). For the male and female variations in MCP-1 levels, it ranges from 10 to 2841 and 22 to 2687 respectively. Likewise, there was no significant relationship in age variations in MCP-1 values (f=0.959, p>0.05).
Conclusions: This study demonstrated no correlation between serum level of monocyte chemoattractant protein-1 with age and gender in polytraumatized patient according to age and gender.

Keywords: MCP-1, Polytrauma, Inflammation, Chemo

INTRODUCTION

MCP-1 is an inflammatory chemoattractant protein that is produced by various cells in the body such as macrophages, fibroblast, epithelial cells and its production can be induced by cytokines, growth factors and other inflammatory makers.[1,2] It plays a key role in the body's response to injuries.[3-5]

Polytrauma is defined as injury to multiple organ system. Trauma and trauma related injuries are part of the most common cause of hospital admission.[6-9] The highest burden of polytrauma and death resulting from it is commoner among male adults partly due to their versatility and involvement in risky behavioral practices.[6,7] The body's response to trauma is by the initiation of acute inflammation and the recruitment of inflammatory cells to

the site of injury.[10-12] This cascade of events is initially mediated by the polymorphonuclear cells and subsequently by monocytes. The body mounts an immune response involving the cells of both innate and adaptive immunity thereby initiating tissue repair which occurs through a coordinated phase. Inflammatory chemokines such as MCP-1 plays a key role in these processes.[10-12] Although more specifically produced by the basophils and monocytes, its level in the blood can be influenced by interleukin-4 (IL-4), IL-1 and platelet derived growth factor (PDGF).[10,13,14] The MCP-1 along with other inflammatory markers influences the release of other chemokines needed for tissue repair by enhancing the infiltrative ability of the monocytes. Following tissue injury there is an associated rise in the blood level of cytokines and interleukins such as IL-6 and IL-8.[1,15-17] This rise is tremendous in patient with multiple injuries. There are documented evidences that MCP-1 level increases in the body following injury.

Also, an increase in MCP-1 has been demonstrated following brain Ischemia in rodents due to the inflammatory processes that accompany ischemic tissues.[2,18,19] Due to the overwhelming responses of the immune cells to multiple injuries which involves an interplay of ischemia, inflammation, and attempt at repair.[4,20]

So far, there is paucity of documented evidence to suggest or affirm the variation in MCP-1 level based on age and sex of an individual.

This study was aimed at assessing, the changes in MCP-1 protein based on age and sex of a polytraumatized patients.

METHODS

This was a prospective hospital-based studies carried out at University College Hospital (UCH), Ibadan. A tertiary hospital in Western Nigeria which received referrals from other neighboring states.

Included in this study were all polytraumatized patient admitted over a twelve-month period (February 2016 to January 2017), that were at least 18 years old while patients who had received any form of treatment prior to presentation at UCH or who were less than 18 years of age were excluded from the study. Also, polytraumatised patients who were brought in dead (BID) or those that died within 48 hours of admission were exempted.

Ethical consideration

Ethical approval was obtained from the University of Ibadan/University College Hospital ethical review committee (UI/EC/15/0032).

Written informed consents to participate in the study was sought and obtained from patients or relation of patients (if unconscious) or waiver of consent obtained from ethical committee/hospital representative (if there was no relation around) were recruited to participate in the study; informed consent form different from the hospital consent form was used.

Participation was voluntary and patients were not coerced into participating in the study.

Patients were allowed to opt out of the study at any time without prejudice or jeopardy to their treatment.

Sample collection

Polytrauma patients admitted through the accident and emergency department who met the inclusion criteria were recruited into the study and had their blood samples taken into an endotoxin free test tube at 48±2 hours after trauma. Samples taken were centrifuge at 450 nm for 10 min to obtain serum and stored in a refrigerator maintained at -80 degree Celsius until analysis. MCP-1 levels in the serum were estimated through the human MCP-1 ELISA kit. This process was carried out using the ELISA technique based on the producer's guide.

Data analysis and management

The data collected were screened for error, imputed and analyzed using IBM statistical package for the social sciences (SPSS) version 20.0 for windows (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

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 110 patients whose samples were adjudged adequate was assayed for MCP-1; making a response rate of 96.5% approximately. Their data are as shown below.

There were 114 participants in this study, of which 110 samples were considered adequate for MCP-1 assay. Thus, the estimated response rate was 96.50%. Of the 110 samples assayed for MCP-1 levels, 79 (71.80%) and 31 (28.20%) were male and female respectively. All participant were Nigerians with 89 (80.90%) Yoruba, 9 (8.20%) Hausa, 7 (6.40%) Igbo and 5 (4.50%) constitute other tribes. 14 (12.70%) of the participant were 60 years and above, 10 (9.10%) were 50-59 years while 27 (24.50%) were 40-49 (Table 1). Others were 30 (27.30%), 26 (23.60%), 3 (2.70%) belonging to ages 30-39, 20-29, and <20 respectively. There is no significant difference in gender variations in MCP-1 level ($t=-0.935$, $p=0.351$). For the male and female variations in MCP-1 levels, it ranges from 10 to 2841 and 22 to 2687 respectively. The mean

male and female variations in MCP-1 levels were 258.65±401.274 (95% C.I; 168.77–348.53) and 348.68±569.617 (95% C.I; 139.74–557.61) respectively as shown in Table 2.

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) years	39.98±14.369	
Range (years)	18 to 80	
Gender		
Male	79	71.80
Female	31	28.20

Table 2: To evaluate gender variations in MCP-1 levels using independent sample t-test.

Variables	N	Mean	Standard deviation	t-test	95% CI	Min	Max	P value	Remark
Male	79	258.65	401.274	-0.935	168.77 to 348.53	10	2841	0.3519	Not significant
Female	31	348.68	569.617		139.74 to 557.61	22	2687		
Total	110	284.02	454.074		198.21 to 369.83	10	2841		

Table 3: To evaluate Age (in years) variations in MCP-1 levels.

Age group (years)	N	Mean	Standard deviation	95% CI		Min	Max	f-test	P value
MCP-P								0.959	0.447
<20	3	125.67	34.298	40.47	210.87	102	165		
20-29	26	193.73	374.966	42.28	345.18	18	1695		
30-39	30	226.70	505.151	38.07	415.33	22	2841		
40-49	27	429.30	531.729	218.95	639.64	15	2687		
50-59	10	276.80	313.050	52.86	500.74	10	1126		
≥60	14	333.43	423.633	88.83	578.03	65	1664		
Total	110	284.02	454.074	198.21	369.83	10	2841		

There is no significant relationship in age variations in MCP-1 values (f=0.959, p>0.05).

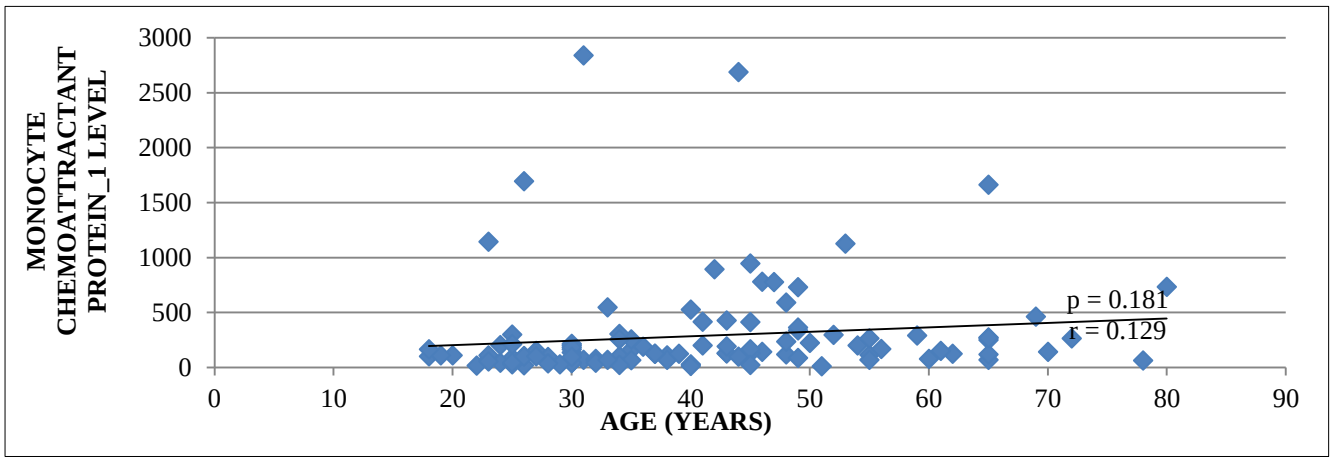

Figure 1: Scatter plot showing the relationship between MCP-1 level and age of patients.

DISCUSSION

Trauma is a global phenomenon and its incidence is on the rise on a daily basis especially in the developing countries where certain factors could be responsible for the higher burden reported in these areas.[6-8] About 32% of reported cases involve injuries to two or more organ systems, increasing the overall odds of death from trauma.[21] Adult males are the most commonly victim of trauma compare to their female counterpart which is reasonable although survival of polytraumatized persons is dependent on various factors ranging from the severity of injury to competency of the host immune system.[6,7,22]

In this study, we investigated correlation of serum levels of MCP-1 in polytraumatized patients with age and gender. This was especially due to the paucity of published clinical data in this aspect.

The findings in this study are in agreement with other studies done in other parts of Nigeria, in Saudi Arabia, India and US respectively.[9,23] In these studies, male adult aged 15-41 were more likely to experience trauma than their female counterpart of same age range. Like other studies, road traffic accident (RTA) and falls were the most common etiologies of trauma of which about 32% sustains injuries involving more than one organ system or with at least a life-threatening condition.

As a pro-inflammatory agent, serum MCP-1 level rises after trauma mediating the release of the pro-inflammatory agents before the onset of tissue healing. Therefore, increase serum MCP-1 is not unexpected.[4,10,24]

Our study showed that serum MCP-1 level in polytraumatized patients was not related to age or gender. This is in consonance with the finding of Jee-Aee et al, in which age and gender were found to be an independent factor associated with MCP-1.[25] To the contrary, in a study titled "increase in circulating levels of monocyte chemoattractant protein-1 with aging", Inadera discovered a rising level of MCP-1 with age.[26] This age–dependent rise in MCP-1 level was presumed to be due to the rise in the oxidative-induced pro-inflammatory markers which increase with age. In the same study, there was a statistically insignicant rise in male MCP-1 levels with males compared to females. The findings by Shelve et al shows evidences suggestive of sex hormone influence on MCP-1 receptor expression.[27] The study showed a significant in vivo suppression of MCP-1 level by estradiol.

Studies have shown that the MCP-4/MCP-1 ratio is invariant over circadian time, and is independent of gender, body mass index or the age at which the trauma was suffered.[27,28] Patient with other co-morbidities such vascular disease and other chronic inflammatory diseases may have a higher serum level of MCP-1 compare to others.[5,11]

According to Frink et al, tissue ischemia secondary to anemia resulting from blood loss which is common in polytraumatized patient, may be associated with increase serum MCP-1 level.[17] Whereas positive correlations of serum MCP-1 base on risk factors for ischemia and inflammation such as hypertension, diabetes and atherosclerosis have been documented in other studies, however, risk assessment was not done in our patient.[26]

During inflammatory processes, available evidences showed a rise in MCP-1 level in other body fluids such as urine and cerebrospinal fluid (CSF).[29] This may be significant in polytrauma patient especially if the injury involved an organ system that regulated the production of the body fluids.

In patient with longstanding diabetic mellitus, there was a proportionate rise in both serum and urine MCP-1 levels. Likewise, serum level glycosylated-albumin and urinary albumin were highly correlated.[30] This, in part, may be due to the persisted glomerular and messangial inflammation sequel to microvascular complication seen in diabetic nephropathy hence the consequent "proteinuria".

According to another study, patient with chronic inflammatory conditions such as osteoarthritis recorded a correlation between serum and CSF concentration of MCP-1 without any age differences.[31,32] In this group of patients there was no gender related correlation in serum MCP-1 level despite a corresponding rise in both CSF and serum MCP-1 in female patient. This, however, is in discordance with the findings in patient with diabetic nephropathy.[30] The rise in the CSF MCP-1 level may suggest the production of MCP-1 by central nervous system specific scavengers such as microglia and astrocytes in response to inflammation.[1,4,10,15] There was no increase in MCP-1 in diabetic patient, contrary to the available evidences. No association was found between serum MCP-1 level with age and gender in patient with ischaemic stroke and myocardium infarction. One of the common and immediate complications suffered by polytraumatize patients is hemorrhage which can result to anemia and reduced tissue perfusion and consequently, ischemia.[17] This is in tandem with a study that demonstrated increase in the expression of MCP-1 receptors in response to localized areas of ischemia in animal studies.[33]

Limitations

Although many studies have been done to correlate monocyte chemoattractant protein in other diseases such as in community acquired pneumonia, vascular diseases, atherosclerosis, morbid obesity, cirrhosis, multiple myeloma, there are still very few documented in this area of study. The selection criteria did not exempt patients with other co-morbidities such as atherosclerosis, diabetic, and hypertension which could have potentially affected the serum MCP-1.

CONCLUSION

This study demonstrated no correlation between serum levels of MCP-1 with age and gender in polytraumatized patients.

Recommendations

Given the current global burden of trauma and the possible upsurge in its incidences in the nearest future and the unique role played by chemoattractant protein in response to inflammation and other immune responses, factors that help for better management and outcome in trauma patient should be further investigated.

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