

The Protective Role of Sickle Cell Anemia in the Pathogenesis of Hypertension in Hyperuricaemic Subjects: A Preliminary Study

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ABSTRACT

The relationship between hyperuricaemia and blood pressure (BP) has been noted for more than half-a century ago. The possible pathogenetic pathway including its ability to induce arteriopathy has recently attracted intense research. Interestingly, sickle cell anaemia (SCA) patients with high prevalence of hyperuricaemia have relatively low BP. This study was thus designed to evaluate the relationship between hyperuricaemia and BP in SCA subjects

SCA patients attending Adult Sickle Cell Clinic who are in stable state with no renal diseases or drugs that could elevate serum uric acid (SUA) were studied. BP measurements were taken in the clinic with a mercury sphygmomanometer at two different visits of 4 weeks interval. The average BP and the mean arterial pressure (MAP) were calculated. Blood samples were taken for SUA, serum creatinine and urea estimations.

Fortynine (49) patients (24 males, 25 females) were studied. Hyperuricaemia was present in 16 (32.6%) of the 49 patients. Their mean ages were 30 ± 9.8 in the hyperuricaemic group and 25 ± 9.5 in the normouricaemic group. The mean of the measured variables were: SUA = 0.51 ± 0.10 (range = 0.43-0.82) mmol/L and MAP = 76.52 ± 7.70 (range = 63.33 - 89.33) mmHg in the hyperuricaemic group. The corresponding values for the normouricaemic group were: SUA = 0.29 ± 0.08 (range = 0.05 - 0.40) mmol/L and MAP = 82.93 ± 12.13 (range = 70.00 - 114.69) mmHg. The BP in the hyperuricaemic group was significantly lower than the normouricaemic group; $t = 2.24$; ($P < 0.05$).

Hyperuricaemia tends to occur in older SCA patients and seems to have an inverse relationship with BP. However the small population studied does

not allow a very strong conclusion on the relationship between hyperuricaemia and BP among SCA patients. A longitudinal study with larger population of SCA patients with hyperuricaemia is recommended

INTRODUCTION

The relationship between hyperuricaemia and blood pressure has been noted for more than half-a century [1-5]. Multiple evidences have emerged enunciating the possible pathogenetic pathway including the ability of hyperuricaemia to induce arteriopathy, glomerular hypertension and subsequently arterial hypertension. This has recently attracted intense research with interesting observations [2-5]. Hyperuricaemia even in pregnant women has been shown to be implicated in children with systemic hypertension who have low birth weight and endothelial dysfunction [6, 7]. Hyperuricaemia has also been suspected to be involved in genesis of hypertension and as a risk factor in the progression of IgA nephropathy [8]. The aforementioned interests among others have further rekindled interest in the relationship between hyperuricaemia and high blood pressure.

Similarly, the association between SCA and hyperuricaemia has been recognized as long as the discovery of sickle cell in the early twentieth century [9, 10]. There have been reports of SCA patients with hyperuricaemia and infrequent association of gout [11-13]. The causes of hyperuricaemia include sustained haemolysis with or without crisis, decreased renal excretion of uric acid, increased purine synthesis and lactic acidemia which inhibits renal tubular secretion of uric acid [11-14]. Paradoxically, SCA patients tend to have a relatively

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low blood pressure in spite of the reported high prevalence of hyperuricaemia.

It is possible therefore that the pathogenetic mechanism of hyperuricaemic-induced hypertension among SCA is different from that in the normal population. The aforementioned observations have rekindled interest in defining the relationship of hypertension, hyperuricaemia in other clinical conditions associated with hyperuricaemia.

There is also paucity of studies that have attempted to look into the relationship of SCA with hyperuricaemia and blood pressure in Nigeria. This study was designed to evaluate the relationship between hyperuricaemia and BP in SCA subjects.

MATERIALS AND METHODS

All consecutive SCA patients who are in stable state attending the Adult Sickle Cell Clinic of the University of Ilorin Teaching Hospital, Ilorin were recruited into the study. Exclusion criteria included use of drugs that could elevate serum uric acid (SUA) and history of renal diseases. All the patients gave voluntary informed consent after due explanation of the concept and procedure of the study. Blood pressure measurements were taken in the clinic with mercury sphygmomanometer at two different visits of 4 weeks interval and the average BP determined. This was used to calculate the Mean Arterial Pressure (MAP) using the formula Diastolic + (Systolic - Diastolic) /3. Blood samples were taken into lithium heparinised bottle for SUA estimations. SUA was estimated by enzymatic spectrophotometric technique. SUA > 0.42 mmol/L was taken to be hyperuricaemia for the purpose of this study. The data was analyzed using Student t-test to determine significance of difference between mean values and Pearson's correlation to determine association between SUA and BP.

RESULTS

Forty-nine SCA (24 males, 25 females) patients seen in the Adult Sickle Cell Clinic of UITH Ilorin were studied. The age range of patients was 15-55 years with mean of 28 ± 9.6 years. Majority of the studied patients 39 (79.6%) were in the age group 15-34 years.

Hyperuricaemia was present in 16 (32.6%) and normouricaemia in 33 (67.3%) of the patients studied. The characteristics of SCA subjects according to level of SUA are shown in Table 1. The mean age in the

normouricaemic group was 25 ± 9.5 while it was 30 ± 9.8 in hyperuricaemic group. However this difference was not significant. The mean SUA of (0.51 ± 0.10) in the hyperuricaemic group was significantly higher than the mean SUA of 0.29 ± 0.08 mmol/L in the normouricaemic group ($p < 0.001$) The mean MAP in the hyperuricaemic group was 76.52 ± 7.70 mmHg (range of 63.33 - 89.33) and in the normouricaemic group 82.93 ± 12.13 mmHg (range of 70.00 - 114.69). Thus the mean MAP was significantly lower than that in the normouricaemic group $p < 0.05$. However, there was no linear correlation between SUA and MAP in this study ($r = 0.47$). The mean MAP in the two groups is depicted in fig 1. The characteristic of SCA subjects according to sex are shown in Table 2. There were 6 males and 10 females in the hyperuricaemic group with mean ages of 29.0 ± 8.70 and 31.80 ± 10.78 respectively. In the normouricaemic group there were 18 males and 15 females with mean ages of 27.0 ± 10.0 and 23.0 ± 8.70 respectively. The differences in the means of their ages were not significant, $p > 0.05$. The mean SUA in males with hyperuricaemia group was 0.49 ± 0.06 and it was significantly higher than that of the females with SUA of 0.12 ± 0.01 .

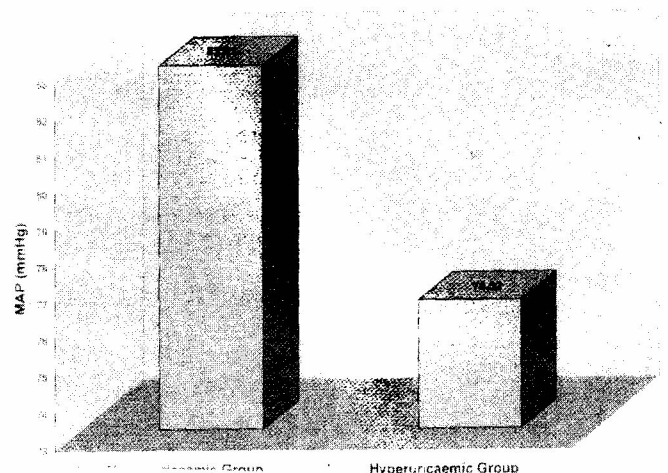


Fig. Mean Artrial Pressure(MAP) in SCA Patients

DISCUSSION

The prevalence of hyperuricaemia among our SCA patients was 32.6%. This is comparable to findings by previous workers who reported values of 32-41% [11-12]. The higher prevalence observed by Gold *et al* was due to a lower cut-off value of SUA used to define hyperuricaemia in their studies [11].

Hyperuricaemia was noted to be commoner among the older age group but not statistically

significant. The reason for this is not clear. It is unlikely to be due to renal impairment consequent upon long duration of the disease as there was no evidence of renal impairment from the measured renal functions[15-16]. Previous report has shown that age is an independent determinant of blood pressure in sickle cell anaemic patients[17]. Probably the corollary holds for hyperuricaemia in SCA.

may result in enhanced NO production with consequent decrease in peripheral resistance. They even postulated that the sickle cell gene could be a marker for blood pressure[16-21]. This may have contributed significantly to the observed low blood pressure in SCA[7-9]. It is possible that the enhanced production of NO reported in SCA has attenuated

Table 1: Characteristics of Sickle Cell Patients According to Levels of Serum Uric Acid

Parameters	Normouricaemic	Hyperuricaemic	p
	n = 33	N = 16	
Age (years)	25 ± 9.5	30 ± 9.8	> 0.05
MAP (mmHg)	82.93 ± 12.13	76.52 ± 7.70	< 0.005
SUA (mmol/L)	0.29 ± 0.08	0.51 ± 0.10	< 0.001

The level of P < 0.05 is significant.

Table 2: Characteristics of SCA Subjects According to Sex

Parameters	Normouricaemic		p	Hyperuricaemic		p
	M	F		M	F	
	n = 18	n = 15		n = 6	n = 10	
Mean Age (yrs)	27.00 ± 10.00	23.80 ± 8.70	> 0.2	> 0.02	31.80 ± 10.78	> 0.02
Mean MAP (mmHg)	82.04 ± 10.04	82.89 ± 14.99	>0.50	> 0.05	75.50 ± 6.21	>0.05
SUA (mmol/L)	0.28 ± 0.07	0.31 ± 0.09	>0.20	< 0.01	0.12 ± 0.1	< 0.01

The level of P < 0.05 is significant

Interestingly, we found in this study that BP is significantly lower among hyperuricaemic than normouricaemic SCA patients. This is in contrast with the recent findings in normal population in which mild hyperuricaemia has been shown to promote arterial hypertension[2-5, 18].

Hyperuricaemia has been shown to be associated with endothelial dysfunction and lower levels of nitrite/nitrate. This consequently leads to lower production of nitric oxide (NO)[18]. In this study the lower BP is consistent with reports of earlier workers that suggested that constant and continuous release of nitric oxide as a result of shear effect of the rigid sickled red cells on the vascular endothelium

the expected effects of increase in blood pressure due to hyperuricaemia.

The result of this study shows that sex does influence hyperuricaemia in SCA. Mean SUA was significantly higher in males than females in the hyperuricaemic group in contrast to the normouricaemic group where the differences were not significant. This is in agreement with the findings of Morgan *et al* who found that the prevalence of hyperuricaemia is significantly higher in males than females[21]. The differences however do not translate to any differences in the blood pressure within the two groups. In this study, there is no linear correlation between BP and SUA. This is in contrast to with

reports of high blood pressure in normal individuals with hyperuricaemia [2, 22-23]

Our findings call for further studies on the relationship between hyperuricaemia and blood pressure in SCA and in other conditions associated with hyperuricaemia. This is necessary to determine if the relationship between BP and hyperuricaemia in SCA is dependent on factors other than the already identified pathogenetic mechanisms. The small size of the study population does not allow for a very strong conclusion in this study. However a longitudinal study with larger population of SCA patients with hyperuricaemia is needed to unravel the relationship and possible reasons why lower BP occurs in SCA with hyperuricaemia.

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