

<https://doi.org/10.46344/JBINO.2020.v09i04.26>

## ENCOURAGING NUTRITIONAL DIET OF CAJANUS CAJAN MAY SIGNIFICANTLY REDUCE SICKLE CELL ANAEMIA

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### ABSTRACT

Sickle Cell Anaemia SCA is the commonest hemoglobinopathy that ravages most part of the world, particularly Nigeria. First-line clinical management of SCA uses hydroxyurea, folic acid, amino acids supplementation, penicillin prophylaxis, and antimalarial prophylaxis to manage the condition and blood transfusions to stabilize the patient's hemoglobin level. These are quite expensive and have attendant risk factors. However, a bright ray of hope involving research into anti-sickling properties of locally available medicinal plants like *Cajanus cajan*. In this study, we investigated the effect of dry seeds of *Cajanus cajan* in a cohort of 37 patients attending sickle cell clinic in Central Hospital Kwale and Ughelli by encouraging their consumption of *Cajanus cajan* after overnight soaking and preparation. While this lasted, their packed cell volume (PCV), frequency of pain crisis, and frequency of admission were monitored, while comparing these parameters with previous hospital records of the same subjects prior to commencement of the study. Our results proved that *Cajanus cajan* significantly decreased the frequency of bone crisis and hospital admission among the patients, averaging 1.95 and 0.57 respectively. Result (differences in means using student t-test) also returned a statistically significant improvement (at  $p < 0.05$ ) in the steady state of PCV values for SCA sufferers from an average of 22.16 to 24.32., suggestive that a mean consumption rate of 3 meals per week is most likely acceptable with minimal side effects. Thus, it is recommended that the burden of sickle cell anaemia be significantly reduced by encouraging a nutritional (sickle cell) diet of *Cajanus cajan*.

**Keywords:** Anaemia, Sickle cell, *Cajanus cajan*, Nutrition

**No: of Tables: 07**

**No: of References: 19**

## Introduction

Sickle cell disease (SCD) is a monogenic public health ailment that affects millions of people across the globe. It is caused by an A-to-T point mutation in the  $\beta$ -globin of the human gene that leads to the production of abnormal haemoglobin called HbS [1, 2]. The gene defect is a single nucleotide mutation single-nucleotide polymorphism (GAG codon changing to GTG) of the  $\beta$ -globin gene, which results in glutamic acid (E/Glu) being substituted by valine (V/Val) at position 6, hence it can be said that the key missing component in sickle cell disease is glutamic acid, glutamic acid is a non-essential amino acid hence the body can produce it however with the defect of haemoglobin its production is compromised [3]. Glutamine is a conditionally essential amino acid, meaning that although the body normally makes sufficient amounts, at times of stress the body's need for glutamine increases, and in such instances, it also relies on dietary glutamine to meet this demand [4].

*Cajanus cajan* is said to be the 6<sup>th</sup> most important legume in the world with various nutritional and environmental properties [5]. One of which is the very high level of glutamic acid, therefore, it is thought that the consumption of *Cajanus cajan* can provide the necessary level of glutamate and hence lead to a reduction in sickle cell crises and the overall global burden of the disease [6].

The greatest burden of SCA is reportedly in sub-Saharan Africa (SSA), where 75% of the 300,000 global births of affected children live and estimates

suggest that 50–80% of these patients will die before adulthood [7, 8], majority of these deaths are in the under-five age group. The morbidity of SCA is enormous and includes embolic strokes, vaso occlusive crises, anaemia, splenic sequestrations, acute chest syndrome etc. Treatment is mainly symptomatic and management of complications. Bone marrow transplantation shows some potential in providing a cure however, it has several complications and a high mortality rate.

Until 2007 Hydroxyl urea has been the de facto drug approved by the US Food and Drug administration agency (FDA) for the treatment of sickle cell disease. The side effects of hydroxyurea are one of the most important concerns. Since some experiments reported several adverse events in patients treated with Hydroxylurea, indicated dermatologic (39.28%), neurologic (23.2%), gastrointestinal (17.5%) and hematologic (10.71%) events in patients with thalassemia and sickle cell disease [9].

In 2007, L-Glutamate was approved by the US FDA for the treatment of sickle cell after a phase III trial. It was found to have an ameliorating effect on sickle cell patients with minimal side effects. Pigeon peas (*Cajanus cajan*) is a locally available and cheap legume with a high amount of glutamate and folic acid, as well as vitamins, minerals, fibres and other amino acids, therefore the potential to reduce the frequency of crises, morbidity and mortality of sickle cell disease [9, 10]. It can be incorporated into the diet of patients hence compliance will be higher

than when patients are compelled to take medications. Side effects will also be limited since it is a natural food.

### **Aim of Study**

This study assessed the ameliorating effect(s) and nutritional value of pigeon peas (*Cajanus cajan*) in the management of sickle cell disease. Specifically, the study;

- i. Determined the lowering effect of *Cajanus cajan* on the rate of hospital admission of sickle cell disease sufferers.
- ii. Investigated if consumption of *Cajanus cajan* can help to increase the Packed Cell Volume of sickle cell patients.
- iii. Examined the relationship between *Cajanus cajan* consumption rate and the reduction in the number/frequency of crises in sickle cell subjects.

### **Materials and Method**

#### **Study Design**

Study was a retrospective cohort study looking at the sickle cell clinic at Kwale Central Hospital and Ughelli Central Hospital since their inception in Delta State, Nigeria. The study was also of the quasi-experimental design as pigeon peas (*Cajanus cajan*) was introduced to the sickle cell patients that made up the cohort. The Control group comprised of subjects within the first three years from inception to commencement of the study, there was also a pre-recorded pre-test and post-test of their Packed Cell Volume(PCV) records and their

frequency of hospital admissions and frequency of crises.

#### **Scope of Study**

Study was conducted in Kwale Central Hospital and Ughelli Central Hospital of Delta State, Nigeria. The study was limited primarily to patients attending sickle cell clinic in the aforementioned hospitals in an attempt to boost the sample size

#### **Study Population**

All patients with sickle cell disease attending in Central Hospital Kwale and Central Hospital Ughelli, including those who attended the general outpatient clinic and those that attended the sickle cell clinic.

#### **Sample Size**

All patients attending the sickle cell clinic who agreed to partake in the study, due to the small size of the study population.

#### **Sampling Technique**

Purposive sampling was used as only patients who were willing and available during the time of study were co-opted into the study.

#### **Exclusion Criteria**

The study excluded patients less than five years old, those unwilling to participate in the study as well as all those who started the clinic less than two years ago.

#### **Inclusion Criteria**

All patients attending the clinic in the last four years, and agreed to be part of the research

### Method and Instrument of Data Collection Research instruments

Hospital data was used for the study. We used data from the sickle cell clinic register, in patient register, and PCV records from their files over the past four years of commencement of the sickle cell clinic. The first three years before the introduction of the pigeon peas served as the control. And this was compared to the first year of taking the pigeon peas. Participants and their parents were counselled on the specific objectives of the study and shown a sample of the pigeon pea and encouraged to consume as frequently as possible while keeping a weekly record. These records were collated monthly when they came for their clinic. At every monthly clinic a packed cell volume (PCV) was obtained to establish the stable state PCV. The stable state PCV is the PCV of the patient when there is no illness. In-patient records were used to obtain the number of

bone pain crises either necessitating admission or outpatient care and the number of admissions due to other illness. The severity of painful crises could not be objectively ascertained

### Reliability of Instrument

The reliability index was determined using Cronbach's alpha test of internal consistency (SPSS Version 22)

### Validity of Instrument

The validity was provided by hospital records.

### Ethical Consideration

Informed consents were taken from patients and their parents/care givers where applicable.

Ethical approval was also gotten from the Delta State Ministry of Health.

### Method for Data Analysis

Data was manually selected and coded for analysis using statistical package for social science (SPSS) version 21. It was summarized using descriptive statistical and chi square test of association between categorical variables.

## Results

**Table I: Distribution of Sickle Cell Anaemia Sufferers by Age and Gender**

S/N	AGE	SEX	FREQ OF CONSUMPTION	FREQ OF BONE CRISES/YEAR		STABLE STATE PCV		FREQ OF ADMISION	
			MEALS/WEEK	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
1	14	M	4	3	1	24	27	3	1
2	8	F	2	1	NIL	26	27	1	NIL
3	15	F	4	1	NIL	23	26	1	NIL
4	18	F	4	NIL	NIL	27	30	NIL	NIL
5	7	M	2	3	1	24	25	3	1
6	11	F	2	3	1	25	26	3	1

7	12	M	3	2	NIL	23	25	2	NIL
8	17	M	3	3	1	20	22	3	1
9	5	F	3	1	NIL	24	26	1	NIL
10	8	F	3	2	NIL	21	23	2	NIL
11	8	F	2	3	1	19	20	3	1
12	5	M	3	3	1	18	20	3	1
13	21	M	3	3	1	22	24	3	1
14	11	F	4	1	NIL	25	28	1	NIL
15	24	F	3	3	1	23	25	3	1
16	15	F	4	2	1	21	24	2	1
17	9	F	4	3	1	24	27	3	1
18	14	M	3	2	1	20	21	2	1
19	3+	M	3	1	NIL	20	22	1	NIL
20	17	F	3	NIL	NIL	26	28	NIL	NIL
21	14	F	2	1	1	19	20	1	1
22	17	F	2	2	1	18	19	2	1
23	7	F	2	2	1	19	20	2	1
24	7	M	3	2	NIL	18	21	2	NIL
25	8	M	4	2	NIL	20	23	2	NIL
26	22	M	3	2	1	21	23	2	1
27	21	M	4	NIL	NIL	27	30	NIL	NIL
28	25	F	4	2	1	23	26	2	1
29	4	M	3	2	NIL	20	22	2	NIL
30	20	M	3	2	1	22	25	2	1
31	8	F	2	3	1	20	21	3	1
32	15	F	3	1	NIL	23	25	1	NIL
33	6	M	4	2	NIL	22	25	2	NIL
34	11	M	3	3	1	23	26	3	1
35	12	M	4	2	NIL	26	29	2	NIL
36	10	F	4	2	1	20	23	2	1
37	20	M	3	2	1	24	26	2	1

Above result shows the demography of the sickle cell anemia patients used in this study. From the result, most of the patients were female, while very few were males.

**Table II: Percentage Distribution by Gender of SCA Patients**

Gender	Frequency	Percent
Male	18	48%
Female	19	52%
Total	37	100%

**Table III: Percentage Distribution by Age of SCA Patients**

	N	Mean	Std. Deviation
Age of patients	Male	12.44	
	Female	12.89	
Total	37	12.67	5.98

**Table IV: Meal of pigeon peas per week**

Meal of Pigeon peas per week	N	%
2	8	21.6
3	17	45.9
4	12	32.4
TOTAL	37	100.0

From tables II, III and IV (above), 18(24.3%) (Table 4.01). The table also shows that, the average age of the patients is approximately 12.7yrs, while their ages Range from 3yrs to 25yrs. On the number of meals per week, Table IV shows that 21.6% of the patients take pigeon peas 2 times in a week; 32.4% of them take it 4 times in a week, while most of the SCA patients (45.9%) take it 3 times in a week.

**Table V: Sample T-test between the Frequency of hospital Admission of Patients before and after the consumption of Pigeon Peas**

Time	N	Mean	SD	Paired Differences				t-test statistics		
				Mean	SD	CI (lower)	CI (upper)	T	df	P
Before	37	1.95	0.91	1.38	0.68	1.15	1.61	12.31	36	0.000
After	37	0.57	0.50							

Table V shows that there was a significant difference in the frequency of admission before ( $1.95 \pm 0.91$ ) and after ( $0.57 \pm 0.50$ ) the consumption of Pigeon Peas ( $df=36$ ),  $t = 12.31$ ,  $p = 0.00$ ). the result shows that before the intervention, the sickle cell patients are admitted on the average of twice, but after the intervention, they barely were admitted in the hospital. The result therefore shows that the consumption of pigeon peas significantly reduces the rate of admission of sickle cell patients.

**Table VI: Sample T-test between the Steady State PCV of Patients before and after the consumption of Pigeon Peas**

Time	N	Mean	SD	Paired Differences				t-test statistics		
				Mean	SD	CI (lower)	CI (upper)	T	df	P
Before	37	22.16	2.62	-2.16	0.80	-2.43	-1.90	-16.44	36	0.000

After	37	24.32	2.95							
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Above table shows that there was a significant difference in the Steady State PCV before ( $22.16 \pm 2.62$ ) and after ( $24.32 \pm 9.95$ ) the consumption of Pigeon Peas ( $t(36) = -16.44, p = 0.00$ ). The result shows that before the intervention, the mean Steady State PCV of the participants is 22.16, but after the intervention, the Steady State PCV increased to 24.32, with a mean difference of -2.16. The result therefore shows that the consumption of pigeon peas increases the Steady State PCV of sickle cell patients. (the negative sign is a result of the lower value in the before intervention score which is subtracting a higher value of the after intervention score)

**Table VII: t-test and frequency of Bone Pains Crisis of Patients before and after the consumption of Pigeon Peas**

Time	N	Mean	SD	Paired Differences				t-test statistics		
				Mean	SD	CI (lower)	CI (upper)	T	df	P
Before	37	1.95	0.91	1.38	0.68	1.15	1.61	12.31	36	0.000
After	37	.57	0.50							

Table VII shows that there was a significant difference in the frequency of Bone Pains Crisis before ( $1.95 \pm 0.91$ ) and ( $0.57 \pm 0.50$ ) after the consumption of Pigeon Peas ( $t(36) = 12.31, p = 0.00$ ). The result shows that before the intervention, the sickle cell patients had an average of bone pain crisis twice a year, but after the intervention, the bone pain crisis reduced to an average of 0.6 per within a year. The result therefore shows that the consumption of pigeon peas reduces the frequency of bone pain crisis of sickle cell patients.

**Discussion**

Pigeon peas (*Cajanus cajan*) is a locally available and cheap legume with a high amount of glutamate and folic acid, as well as vitamins, minerals, fibres and other amino acids, therefore the potential to reduce the frequency of crises, morbidity and mortality of sickle cell disease. It can be inco-operated into the diet of patients hence compliance will be higher than when patients are compelled to take medications. In this study, the ameliorating effect(s) and nutritional value of pigeon peas in the management of sickle cell disease was investigated. From our study, the mean age of the participants was  $12.67 \pm 5.98$  years with a slightly lower male to female

ratio of 18:19. The males were also slightly younger than the females with a mean age of 12.44 years compared to 12.89 years. The mean consumption was 3 times weekly with 8 of them eating twice a week, 17 eating 3 times weekly and 12 eating 4 times weekly.

The finding on frequency of admission per year of patients before and after one year of consuming pigeon peas showed a statistically significant decrease from 1.95 admission per year  $1.95 \pm 0.91$  ( $p = <0.05$ ) before to less than one per year i.e.  $0.57 \pm 0.50$  ( $p = <0.05$ ) after. When compared to results of 4.75 before treatment to 2.25 with a confidence interval of >95% after treatment with use hydroxyurea [11]. One of the hallmarks of

sickle cell disease is anaemia due to the shortened lifespan of HbS (40-50days) compared to an average of 120days for HbA.

For this study, the steady state PCV was taken as the PCV level when the patients are free of illness for 2 weeks and was usually taken when the patient came for routine clinics which was monthly, with most patients having over six visits a year. The study showed a statistically significant increase in the steady state PCV from a mean of  $22.16 \pm 2.62$  ( $p = <0.05$ ), to  $24.32 \pm 2.95$  after taking pigeon peas meals for just one year. This is comparable to a study using hydroxyurea, where Hemoglobin (g/dL) increased from  $8.15 \pm 1.30$  to  $8.77 \pm 1.240$   $p=0.01$  [12]. The steady state PCV is also in keeping with a report that most patients (57.1%) had hemoglobin between 7-10 g/dl and 63.3% had packed cell volume between 20-30%. Only 11.2% had hemoglobin greater than 10 g/dl and 12.2% had packed cell volume greater than 30%. While 31 (31.6%) had hemoglobin less than 7 g/dl and 24 (24.5%) had packed cell volume between 13-20%. Mean Hb level in males was  $8.14 \pm 1.54$  and in females was  $7.73 \pm 1.45$  ( $p=0.8$ ). The mean PCV in males was  $25.1 \pm 4.9$  and in females was  $23.9 \pm 4.6$  ( $p=0.6$ ) [2, 13].

The most dramatic presentation of Sickle Cell Anaemia is the Bone pain crisis which affects the back, femur, tibia., digits, abdomen, etc. Vaso-occlusive pain episodes are the hallmark of sickle cell disease that is most commonly manifested by bone pain. Individuals with SCD experience recurrent pain episodes, and up to 30% of patients

report daily symptoms. Sickle cell disease pain may last for hours to days, and some SCD individuals are never completely pain-free [14].

The findings showed a mean of  $1.95 \pm 0.91$  ( $p = <0.05$ ), before commencement of the study reducing to  $0.57 \pm 0.501$  ( $p = <0.05$ ), after a year of consuming pigeon peas, a 71% reduction in the median number of pains per year. This result was even more significant than a study done in a multicentre study using hydroxyurea in sickle cell anaemia, which enrolled patients with SCD  $\geq 18$  years of age, hydroxyurea was associated with a 44% reduction in the median number of pain episodes per year compared to the placebo (4.5 vs. 2.5,  $P < 0.001$ ) as well as a reduction in the median number of pain episodes requiring hospitalization (2.4 vs. 1.0 per year,  $P < 0.001$ ) [15].

These findings are also similar to that of Akinsulie, Temiye, Akanmu and Lesi (2005) who in their study on 100 sickle cell patients that were given the extract of *Cajanus cajan* and monitored for six months found that extracts of pigeon pea reduced the bone pains of sickle cell patients that were sampled [16]

*Cajanus cajan* has also been found to be potent and relatively safe for use in preventing sickle cell crisis [17]. Fernandes (2017) reported that the percentage of sickled cells before the laboratory experiments was 91.6%, but that decreased with treatment with *C. cajan* seed (41.7%), *C. cajan* leaf (32.8%), in a study on laboratory animals [18]. Cordovil (2015), reported that in Brazil, detailed studies with pigeon peas chemical-biological may clarify the



mechanisms by which the inhibition of sickling of red blood cells occurs, reducing oxidative stress and thus helping treating people affected by this disease [19].

### Conclusion

Eating of pigeon peas (*Cajanus cajan*), at a rate of three meals per week over a period of one year by thirty seven patients with a mean age of 12.67yrs attending sickle cell clinic in Central Hospital kwale and Central Hospital Ughelli and using the first three years of not eating the pigeon peas while attending the sickle cell clinic as a control, showed a statistically significant ameliorating effect on the steady state PCV, number of bone crises and number of hospital admissions in both males and females and was generally well tolerated. The high level of Glutamate and folic acid may play a role in these ameliorating effects of pigeon peas however other nutrients may also be responsible

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