

Pregnancy in sickle cell disease patients: a single centre study

Abstract

Background: In Nigeria, there is a gradual improvement in Health care delivery in the past three decades, this has also impacted positively on the live span of Sickle cell disease with increasing number of the females attaining the age of marriage and becoming pregnant. This however, poses obstetric complications if pregnancy progresses without adequate care and follow-up. This study aimed at determining the prevalence and challenges of SCD pregnant women seen in ante-natal clinic in Port Harcourt, River state (South-south region) Nigeria.

Methodology: This was a ten years retrospective study, conducted at Braithwaite Memorial Specialist Hospital, Port Harcourt. The Subjects were seen at the Ante-natal Clinic of the Hospital and a total of 35,976 pregnant women had their ante-natal care and delivery at the hospital from January 2003-January 2013. All the patients were screened for SCD, on enrollment for ante-natal care. Other relevant investigations were also carried out including Full blood Count, Genotype, Electrolyte, Urea, Creatinine, Fasting blood sugar, abdominal Ultrasound and Urinalysis. Data analysis was obtained using Statistical software Epi-info version 7.02 by WHO, Geneva, Switzerland and CDC, USA.

Result: A total of 35,976 pregnant women were seen at the ante-natal clinic within the study period. Twenty eight thousand, eight hundred and fifteen (80.09%) of women were Hb AA, 7,109(19.77%) were Hb AS and 52 were Hb SS (prevalence of 1.4 per 1000 pregnant women). The average booking gestational ages of 22.2 and 29.1 weeks were recorded for SCD and non-SCD participants respectively. The Tertiary level of education was relatively higher among the SCD (60%) compared to non-SCD (58.05%) population, although this was not statistically significant. A total of 13,276(39.2%) and 49(94.2%) of non-SCD and SCD respondents respectively had Hb concentration below 11g/dl (anemia) ($P=0.001$).

Conclusion: The prevalence of sickle cell disease in pregnancy is on the gradual increase in this region, probably due to improving Health care provision in Nigeria. A common challenge among the SCD patients is that more than 94% had Hemoglobin level below 11g/dl which may pose some challenge in successful management of the patients.

Keywords: pregnancy, haemoglobinopathy, acute-chest syndrome, vaso-occlusive, hyper-hemolytic, aplastic, chronic anemia

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Abbreviations: SCD, sickle cell disease; BMSH, braithwaite memorial specialist hospital; LBW, low birth weight; IUFN, intra-uterine fetal death; SPDC, shell petroleum development company; VDRL, venereal disease research laboratory; HBsAg, hepatitis b surface antigen; TBAs, traditional birth attendants; ACSM, advocacy, communication and social mobilization; GIS, geographical information system

Introduction

One of the greatest public health problems of our time is that due to sickle cell disease, a genetic disease of the globin chain of the red blood cells.^{1,2} It affects millions of people throughout the world and is commoner among those whose ancestors came from sub-Saharan Africa.³ In West and Central Africa where it is the commonest hemoglobinopathy, 25% of the people have sickle cell trait while 2-3% of all babies are born with a form of the disease. It is estimated that sickle cell occurs in 1 out of every 500 African.⁴ In United States, an estimated 80,000-90,000 Americans of African extraction are affected

by sickle cell disease, while about 3million have sickle cell traits.⁵ In Nigeria, about 45,000-90,000 babies with sickle cell disease are born annually as against 1000 babies born in United States.^{4,6}

The sickle cell (SC) gene disorder occurs in high frequency in endemic malaria regions especially in the Plasmodium falciparum pressure belt, low and middle-income countries.⁷ These areas account for three-quarter of an estimated 300,000 to 500,000 children born with SC disease worldwide every year. The high prevalence stems from an evolutionary link between the SC gene and resistance to malaria, a feature that also underpins the common inclusion of sickle cell screening in health research in malaria endemic zones where the gene may act as a risk factor.^{3,8}

Sickle cell disease is reported to be associated with a very high rate of childhood mortality.⁹ It contributes to 5% of under-5 death on the African continent. Other health problems include: decrease in median survival, chronic anemia, end-stage renal failure, acute-chest syndrome, vaso-occlusive, hyper-hemolytic, aplastic and

sequestration-crises.¹⁰ All these complications pose significant threats to public health in the management of sickle cell disease, especially in economic constrained settings in Sub-Saharan African countries.

Pregnancy in patients with sickle cell disease is associated with increased maternal and fetal morbidity and mortality. Maternal complications may include recurrent anemia, bone pain crises, recurrent malaria infection, acute chest syndrome, spontaneous abortion, lobar pneumonia, infections, pseudo toxemia, hemolytic crises, pre-eclampsia, retained placenta and maternal death just to mention a few. The fetal complications may include: low birth weight (LBW), Intra-Uterine Fetal death (IUFD), Stillbirth, breech presentation, etcetera.^{11,12}

Although progress has been made in the management of sickle-cell disease in high-income countries over the past one decade, in most middle and low-income countries where sickle cell disease is a major public health problem, its management has remained inadequate.¹⁰ There are no strong national health policies to control sickle cell disease in most Sub-Saharan African countries. In most cases the basic facilities needed to screen, diagnose or manage the patients are usually absent. More often, diagnoses are first made when complications have set in.⁸ Without early diagnosis and treatment, pregnant mothers and children with SCD often die due to labor complications and chronic anemia.

This study is aimed at determining the prevalence of SCD pregnant women in Port-Harcourt River state, South-South Nigeria and the relationship of the hemoglobin variants of the pregnant women with their hemoglobin concentration at booking. The result of this study may be used to generate policy programs that will improve the quality of life of people living with SCD in sub-Saharan Africa.

Methodology

This was a ten years retrospective study, conducted at Braithwaite Memorial Specialist Hospital, Port Harcourt. The Subjects were seen at the Anti-natal Clinic of the Hospital and a total of 35,976 pregnant women had their anti-natal care and delivery at the hospital from December 2003-December 2013. Port Harcourt is an oil-rich cosmopolitan city located in the South-South region of Nigeria. It has an international airport and a sea port. The presence of oil attracted so many oil companies such as Shell Petroleum Development Company (SPDC), Mobil, Chevron, Agip and TotalfinaElf oil companies just to mention a few into the city.

Ethical clearance

It is for the study was obtained from the ethical committee of the Braithwaite Memorial Specialist Hospital (BMSH).

Data collection and analysis

Data was collected through Health Information medical records from the files of the patients at the ante-natal clinic BMSH. There was a hypothesis generation questionnaire which was source of information at the booking clinic for each patient. Hemoglobin variant was obtained through Hemoglobin electrophoresis of patients' venous blood collected at first booking in the antenatal clinic. Data obtained consisted of age, educational status, occupation, gestational age at booking, hemoglobin concentration at booking, blood group, genotype, screening status of HIV, Veneral Disease Research Laboratory (VDRL) and Hepatitis B Surface Antigen (HBsAg) tests.

Statistical analysis

The data were entered and analyzed using Epi-info version 7.02. Statistical analysis of mean and standard deviation were calculated. Student t-test was used to test the significance of differences between mean values. Statistical significance was set at probability (P)≤0.05.

Result

A total of 35,976 women who attended ante-natal clinic of BMSH community, Port Harcourt between December 2003-December 2013 were studied, out of which 28,815(80.09%) were Hb variant AA (Hb AA), 7,109(19.77%) were AS (Hb AS) and 52(0.14%) were SS (Hb SS-homozygous) (Table 1).

Table 1 The genotype (Hemoglobin Variants) of pregnant women at booking clinic

Genotype	Frequency(n)	Percent(%)
AA	28,815	80.09
AS	7,109	19.77
SS	52	0.14
Total	35,976	100

The mean age of SCD pregnant women was 27years with a higher percentage of women (59.6%) in the 20-29years group. A good number of the SCD pregnant women had tertiary level of education (59.6%) while 40.4% had secondary education. Although more SCD pregnant women had tertiary levels of education than the non-SCD counterparts, this was not statistically significant. There was no SCD pregnant woman with primary level of education at booking. Most of the women were civil servants (28.85%), 25% were house wives, 21% were traders, 19% were students while 5.7% were artisans. A total of 24(46.2%) of the SCD pregnant women booked in the second trimester, while 18(34.6%) and 10(19.2%) booked at the third and first trimesters respectively. The average booking gestational ages of 29.1 and 22.6 weeks were recorded for non-SCD and SCD participants respectively. The minimum and maximum gestational ages of booking for the SCD pregnant women were 4 and 36weeks respectively (Tables 2A & 2B).

Table 2A The socio-demographic, obstetric and biomedical data of sickle cell pregnant women at booking clinic

Characteristics	Frequency(%)
Age group	
<20	3(5.77)
20-29	31(59.62)
30-39	18(34.62)
Total	52(100.0)
Education	
Primary	0(0.0)
Secondary	21(40.38)
Tertiary	31(59.62)
Total	52(100.0)

Table Continued....

Characteristics	Frequency(%)
Occupation	
Civil servant	15(28.85)
House wife	13(25.0)
Student	10(19.23)
Stylist	3(5.77)
Trading	11(21.15)
Total	52(100.0)
Blood group	
A. POS	14(26.92)
B. POS	6(11.54)
O. NEG	1(1.92)
O. POS	31(59.62)
Total	52(100.0)
Trimester	
1st	10(19.23)
2nd	24(46.15)
3rd	18(34.62)
Total	52(100.0)

Table 2B Levels of education of pregnant women at booking: SCD compared to Non-SCD pregnant women

Levels of education	Frequency (n)(%)		Total (n %)	p-value
	Non-SCD	SCD		
Primary(1-6)	71(0.2)	0	71(0.2)	
Secondary(1-6)	14,118(41.8)	20(40)	14,138(39.7)	>0.05
Tertiary	19,607(58.0)	32(60)	19,639(57.2)	
Total	33,756(100)	52(100)	33,806(100)	

Note: A random sample of 33,756 non-SCD pregnant women whose levels of education were documented at booking.

The mean hemoglobin concentration of SCD respondents was 8.16 ± 1.58 g/dl. The prevalence of anemia in SCD pregnant women at booking was 94.23% (49), out of this 12.24% had mild anemia (Hb=10-10.9 g/dl), 65.31% had moderate anemia (Hb=7-9.9 g/dl) and 22.45% had severe anemia (Hb<7 g/dl). Anemia in SCD pregnant women was statistically greater than that in non-SCD counterparts ($p<0.05$). A total of 3(5.77%) and 20,554 (60.8%) SCD and non-SCD pregnant women respectively were non-anemic (Hb \geq 11 g/dl) at the time of booking (Table 3A & 3B).

The age group 20-29 had a statistically significant higher anemia than women less than 20(6.12%) and those between 30-39(36.73%) ($X^2=29.08; 0.001$). Most of the tertiary educated women (83.9%) booked earlier (between 1st and 2nd trimesters). However, in those that had only secondary education (38%) booked in the 1st and 2nd trimester and this was statistically significant ($p<0.05$). Women that had tertiary levels of education had statistically significant higher anemia 30(61.22%) than those with secondary levels of education

(38.78%) ($X^2=42.31; 0.001$). There was no statistical significant relationship between anemia and socio-demographic factors ($X^2=8.78; 0.067$). Most of the women were blood group O rhesus D positive (59.6%) followed by A (28.57%) and B rhesus D positive blood groups (11.5%) respectively. The least prevalent blood group was O rhesus D negative (2.0%). Women with O rhesus D positive blood group had statistically significant higher anemia 29(59.18%) than women with other blood groups ($X^2=50.37; 0.001$). The severity of anemia increased as the pregnancy progressed from first (Hb 8.31 g/dl) to third trimester (7.96 g/dl). However, there was no statistically significant association between anemia in SCD pregnant women and gestational age ($OR=0.94$, 95% CI=0.00-14.89, $p=0.73$) (Table 4A & 4B) (Figure 1). The highest hemoglobin concentration was 12 g/dl at 2nd trimester while the least was 5.3 g/dl recorded at the third trimester.

Table 3A The Prevalence and grades of anaemia in SCD pregnant women at booking

Anaemia/grade	Frequency	%
HB(g/dl)		
Anaemic(<11.0)	49	94.23
Non-Anaemic(>11.0)	3	5.77
Total	52	100
Grade		
Mild(10-10.9)	6	12.24
Moderate(7.0-9.9)	32	65.31
Severe(<7)	11	22.45
Total	49	100

Table 3B Pattern of hemoglobin concentrations in SCD and non-SCD pregnant women @booking

Hb concentration (g/dl)	Frequency(n)(%)		Total(n %)	p-value
	Non-SCD	SCD		
<11	13,276(39.2)	49(94.2)	13,325(39.3)	
\geq 11	20,554(60.8)	3(5.8)	20,557(60.7)	<0.05
Total	33,830(100)	52(100)	33,882(100)	

Note: Hb concentration <11.0 g/dl connotes Anemia in pregnancy.^{13,14} A random sample of 33,882 non-SCD pregnant women whose Hemoglobin concentration were documented at booking

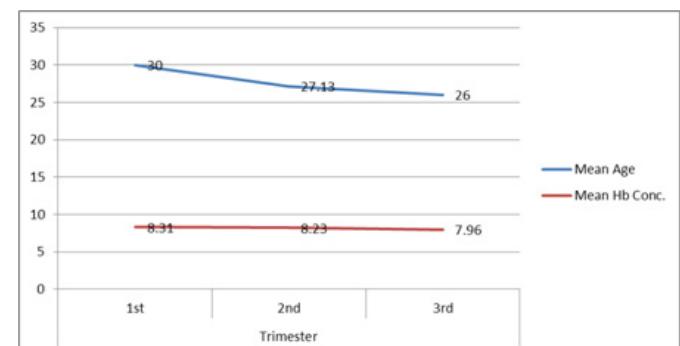
**Figure 1** Line graph showing a decrease in mean age and Hb Conc. of SCD patients from 1st to 3rd trimester.

Table 4A The prevalence/pattern of anaemia according to socio-demography, obstetric factors and blood groups (Biomedical variables) of sickle cell pregnant women at booking clinic

Characters/variables	Anaemic(n %)	Chi-square(p-value)
Age group(years)		
<20	3(6.12)	
20-29	28(57.14)	29.08(0.001)*
30-39	18(36.73)	
Total	49(100.0)	
Education		
Primary	0(0.0)	
Secondary	19(38.78)	42.31(0.001)*
Tertiary	30(61.22)	
Total	49(100.0)	
Occupation		
Civil servant	14(28.57)	
Housewife	12(24.49)	
Trading	10(20.41)	8.78(0.067)
Stylist	3(6.12)	
Student	10(20.41)	
Total	49(100.0)	
Blood Group		
A Rhesus Positive	14(28.57)	
B	5(10.20)	
O	29(59.18)	50.37(0.001)*
O Rhesus Negative	1(2.04)	
Total	49(100.0)	
Gestational Age		
1st trimester(0-13 weeks)	9(18.4)+++	
2nd trimester(14-26 weeks)	23(46.9)++	(OR=0.94, 95% CI=0.00-14.89; p=0.73)
3rd trimester(27-39 weeks)	17(34.7)+	
Total	49(100.0)	

Note: The plus signs connote Hb concentrations [+++ = 8.31g/dl; ++ = 8.23/g dl; + = 7.96g/dl]

Table 4B Cross tabulation of hemoglobin concentrations with genotypes in pregnant women at booking

Hb concentration (g/dl)	Hemoglobin variant (Genotype)		Total(n (%)
	AA	AS	
<11.0	10,262(34.5)	3014(42.7)	49(94.2) (39.3)
>11.0	16,506(65.5)	4048(57.3)	3(5.8) (60.7)
Total	29,768(100.0)	7062(100.0)	52(100) (100.0)

Chi-Square: 188.78, p-value=0.001

Note: A random sample of 33,883 registered pregnant women who had their hemoglobin concentrations and genotypes (Hb variant) documented at booking.

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All the non-anemic SCD pregnant women (5.77%) were within the age range of 20-29years out of which 2 (3.8%) attained secondary levels of education while 1 (1.9%) had tertiary education; each of these subject was either a civil servant (1.9%), house wife (1.9%) or trader (1.9%); 2(3.8%) were O rhesus D positive while 1 (1.9%) was B rhesus D positive blood groups respectively. One (1.9%) of the SCD pregnant women was HIV-1 and 2 sero-positive while none of them was HBsAg and VDRL sero-positive.

Discussion

SCD is the most prevalent genetic disease in the African Region. In many countries, 10%-40% of the population carries the sickle-cell gene resulting in estimated SCD prevalence of at least 2%.⁶ The complications which arise from SCD occur mostly in children under five years, adolescents and pregnant women. Hence, they are referred to as the vulnerable group.

This study showed 0.14% as the prevalence of sickle cell disease in pregnancy in River state. An earlier study in same River state by Ugboma et al.¹⁵ showed a prevalence of 0.2%.¹⁵ From our study, it is estimated that 1 out of every 714 pregnant women seen in the ante-natal clinic in the region will have sickle cell disease. This is relatively lower than the prevalence of 1 out of every 500 African child estimated by SCD global.⁴ This may be due to the fact that many of the affected children die before reaching child bearing age. Also, late menarche and infertility among females with sickle cell disease may play a role. However, a prevalence of 19% sickle cell trait (SCT) was in keeping with other similar studies in this region.^{15,16} Although 52 SCD in pregnancy were documented from this study over a 10-year period, this was higher than that documented by Ocheni et al.¹² in his retrospective study in South-eastern Nigeria. Ocheni et al.¹² document only 10 SCD in pregnancy over a period of 30 years. However, the number of SCD pregnant women was relatively lower than that documented by Odum et al.¹⁷ in which 60 SCD in pregnancy were documented within 3-year period of retrospective study in South-western Nigeria.

The study showed that over 59% of the booked patients in the clinic had tertiary level of education. This was relatively lower than that in previous study by Ugboma et al.¹⁵ where about 80% of the SCD pregnant women who registered in the ante-natal clinic had tertiary education.¹⁵ The absence of women with primary level of education may be as a result of the fact that this group of women prefers local alternatives such as Traditional Birth Attendants (TBAs) in place of comprehensive health care.¹⁸ Empowering women through education could be a strategy of reducing both the maternal and infant mortality rates of these vulnerable groups in our environment. An educated woman would tend to take a wiser and healthier decision than the illiterate/poorly educated woman. Our study was able to show that more SCD pregnant women with higher level of education seek comprehensive health care compared to non-SCD counterpart, though this was not statistically significant. Education, therefore, plays a positive role in improving the quality of lives of people living with SCD during pregnancy. In addition, this study showed that maturity (in terms of age) and social class (in terms of occupation) may play vital role in decision-making on when to register for ante-natal care. This was evidenced by the fact that more older women of higher social classes (i.e. civil servants) booked earlier (1st and 2nd trimesters) than the younger women of lower social classes (i.e. House wives) who booked in their late trimesters (2nd and 3rd trimesters).

The average gestational age of 22.6 and 29.18weeks at booking were noted for SCD and non-SCD pregnant women respectively, these

indicate late booking. This implies that majority of the SCD women registered at the second trimester while the non-SCD counterparts registered at third trimester. The finding showed that SCD pregnant women booked earlier than the non-SCD pregnant women, this was not however, statistically significant ($p>0.05$). Onoh et al.¹⁹ and Ugboma et al.¹⁵ recorded average booking gestational ages of 24.3 and 16.6 weeks respectively in Abakaliki, South-eastern¹⁹ and Port Harcourt, South-southern Nigeria respectively. In our study, it was found that 83.1% of the pregnant women booked after first trimester. This may not be in the interest of the maternal and fetal well-beings. Antenatal care is one of the pillars of SAFE Motherhood Initiative aimed at preventing adverse pregnancy outcome. Early antenatal booking is recommended for this benefit. When a woman books late in the ante-natal clinic, the benefit of safe motherhood is defeated. The advocacy has always been early booking as the panacea for favorable pregnancy outcome. Less than twenty percent of SCD pregnant women registered in first trimester from our study.

The definition used in this study for anemia in pregnancy was based on World Health Organization's definition- hemoglobin concentration less than 11g/dl.^{13,14} This study showed that 94.2% and 39.2% of SCD and non-SCD pregnant women respectively presented with hemoglobin value less than 11.0g/dl. This was similar to the values obtained in previous studies with non-SCD pregnant women in Nigeria by Aluka et al.²⁰ and Adinma et al.²¹ where the prevalence of 40.4% and 40.08% respectively were recorded. Anemia in pregnancy is very common in low and middle income countries. It is one of the greatest burdens of SCD in pregnancy. Pregnant women with sickle cell anemia are classified as high risk. A prevalence of 94.2% in SCD in pregnant women is statistically significant and a hematological emergency. This is because anemia in SCD pregnant woman increases the risk of both maternal and fetal deaths. Maternal death could be due to anemic heart failure, fulminant bacterial and parasitic infections (such as UTI and malaria), acute chest syndrome, shock from blood loss, vaso-occlusive crises hyper-haemolytic crises, toxemia of pregnancy and abortion just to mention a few. Fetal death could be from birth asphyxia, intrauterine growth retardation, intrauterine death, low birth weight, abnormal presentation, and fetal distress.¹² Odum et al.¹⁷ found that antenatal and postpartum blood transfusion rates for the sickle cell disease patient in Lagos, Nigeria were 45.0% and 81.6% respectively.¹⁷ Anemia, evidenced by low hemoglobin concentration could be a predictive marker of women who may require red cell transfusion during ante-partum or postpartum period. It connotes a poor prognosis especially if it is moderate-severe at booking. Our study showed that most SCD pregnant women had moderate-severe anemia at booking. The late booking coupled with severity of the anemia indicate unfavorable pregnancy outcome. Early booking helps the pregnant woman to be acquainted with primary modalities to prevent anemia. For instance, early institution of haematinics such as folic acid, elemental iron supplements and other routine drugs (such as anti-malaria prophylaxis) will go a long way to prevent iron deficiency and megaloblastic anemia which are common types of anemia in pregnancy. This simply explains the reason why most of the women who booked at the second and third trimester had anemia. One of the challenges facing SCD globally is underfunding and lack of publicity. SCD is the single most common life-threatening genetic disease. The cost of managing SCD is so enormous that it is unprecedented, yet it is less funded and less advocated.^{22,23}

SCD is associated with higher childhood mortality in low-income countries compared to high-income and some middle-income countries.^{7,24,25} With the current advances in the management of SCD commoner in high and middle-income countries, the average

lifespan of people living with SCD has improved up to 3-4 decades of life, hence, a transition from mortality to morbidity (burden) of the disease. The implication is that more funds will be channeled towards managing the SCD crises and obstetric complications of SCD in pregnancy. In addition, there is poor Health Information Management system (HIM) in most health centers in Nigeria. This could lead to prolong turn-around-time in information retrieval system. All these are compounded by the absence of national policies for public health planning for people living with SCD.²⁶

SCD is a preventable disease and so our strength to control this disease in sub-Saharan Africa is hinged on Advocacy, Communication and Social Mobilization (ACSM). This forms the conceptual framework for the strategy in carrying out this study. Advocacy in this context connotes deliberate process of influencing those who make policy decisions. It is delivering messages that are intended to influence the actions of policy makers. There is poverty of knowledge about SCD and its impact in the vulnerable groups in sub-Saharan Africa. As a result of this, many of them die due to complications which, under normal circumstances, would have been circumvented. Advocacy will create the awareness and send messages across the appropriate quarters for appropriate interventions to curb this menace. In order to drive SCD research project successively in Nigeria, a team of leaders with political, core transformational, trans-organizational and team competencies are needed. Advocacy and social mobilization rely on communication strategies to ensure community engagement [27]. The ultimate goal is to bring about the desired change which will improve the quality of lives of people living with SCD. In addition, viable health information management system (health informatics) evidenced by proper medical records with detailed demographic information of the participants, geographical information system (GIS), reliable data collection system, community support and a team spirit are the strengths that will drive SCD projects to ensure qualitative implementation of these strategies.

Conclusion

The prevalence of SCD in pregnancy is gradually increasing in sub-Saharan Africa. Late booking, illiteracy, anemia and inadequate treatment are the core indicators of poor pregnancy outcome in low-income countries such as Nigeria. There is need to create the awareness through media network, involving the government and other donor agencies in order to institutionalize appropriate health interventions aimed at early detection (diagnosis), early booking for ante-natal care and treatment of people living with SCD. This will impact positively on the quality of lives and pregnancy outcome of SCD mothers. Female education must be regarded as a topmost priority in order to achieve this goal. The government, as a matter of urgency, must enact a national policy that will support the care of people living with SCD in Nigeria. These strategies, if implemented, will go a long way in reducing the burden of SCD and ultimately create a SCD-free society.

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Conflict of interest

The author declares no conflict of interest.

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