
PACIFIC JOURNAL OF MEDICAL SCIENCES



VOLUME 14, No. 2, April 2015

PACIFIC JOURNAL OF MEDICAL SCIENCES
{Formerly: Medical Sciences Bulletin}
ISSN: 2072 – 1625



Pac. J. Med. Sci. (PJMS)

www.pacjmedsci.com. Email: pacjmedsci@gmail.com.

ISSN: 2072 – 1625

Volume 14, No. 2, April 2015

A multidisciplinary journal for publication of medical and biomedical research findings on issues pertinent to improving family health and related issues of public health

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AN ASSESSMENT OF SOCIODEMOGRAPHIC AND BIO-CLINICAL CORRELATES OF HIV INFECTION IN PREGNANCY IN SOUTHERN NIGERIA: A RETROSPECTIVE STUDY.

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ABSTRACT:

Human immunodeficiency virus (HIV) infection is a global pandemic with frightening mortality and morbidity, no effective vaccine and curative treatment though it is preventable. Globally heterosexual and vertical transmissions remain the leading means of its spread. The sub Saharan African female adults are the most affected and most of the world HIV positive children were from vertical transmission. Therefore an in-depth knowledge of the women HIV risk factors is crucial to its effective prevention and control. The general objective of this study was to investigate the association between sociodemographic and bio-clinical variables and HIV infection in pregnancy. The specific objectives were to determine the prevalence of HIV infection among pregnant women and to compare the sociodemographic profiles and the bio-clinical variables of HIV seropositive mothers and matched seronegative counterparts. This was a retrospective case control analysis of 116 HIV positive mothers as study group and 232 HIV negative mothers as control group. The data used was obtained from the records of women that delivered between 2009 and 2013 in a mission hospital, in Benin City, Edo state, South-south, Nigeria. Statistical analyses of the data were done, P-value of 0.05 was considered as significant. Our results indicated that the prevalence of HIV seropositivity in pregnancy in this setting was 2.94%. HIV Seroprevalence was statistically significant different among women aged 25-29 years ($p=0.048$) and 30-34 years ($p=0.01$), with low (primary) educational attainment ($p=0.048$) and in government employment (OR.0.25, $P=0.006$). The seropositive mothers had significantly lower haematocrit ($P=0.0015$), higher incidence of anemia at booking ($P=0.0023$) and reduced weight gain at term ($P=0.013$). Their newborns significantly weighed less at birth ($P=0.0032$), suffered intrauterine growth restriction ($P=0.0002$) and low birth weight ($P=0.0017$). HIV infection in pregnancy is still a significant burden. It appears to have social predictors and materno-fetal health implications. We therefore recommend sustained efforts at personal level especially behavioral and lifestyle adjustment, collective and at government level female gender empowerment to control the scourge.

Key words: HIV infection, pregnancy, socio-clinical, correlates, Nigeria

Submitted: August 2014; Accepted: January 2015

INTRODUCTION:

Acquired immune deficiency syndrome (AIDS) is a pandemic of acquired defect of the cellular immune system [1] caused by human immunodeficiency viruses (HIV) 1 and 2 [1-3]. It was first diagnosed in 1981 and the first case was reported in Nigeria in 1986. HIV currently affects all races, ages and genders. HIV is the global leading infectious killer. Estimated 36 million people have died from it since its onset and 1.6 million people died in 2012 alone according to World Health Organization (WHO) [4]. In 2009, 22.5 million (68%) of an estimated 33.3 million people living with HIV/AIDS were in sub-Saharan Africa. 1.8 million of the 2.6 million global new infections were in sub-Saharan Africa [5] and 1.8 million of 2.1 million peak of 2004 AIDS-related mortality was in the sub region. Adult prevalence among people aged 15-49 years was 5% in sub-Saharan Africa [5] while global figure was 0.8%. This stems from high heterosexual transmission coupled with high male-female ratio and high total fertility rate in the sub region. Currently some 35.3 million people globally are living with HIV/AIDS; about 95% of new infections affect individuals living in low and middle income nations particularly in sub-Saharan Africa with about 69% of global HIV/AIDS burden [4].

As at 2009 Nigeria along with Ethiopia, South Africa, Zimbabwe and Zambia were the countries with leading HIV/AIDS epidemics in sub-Saharan Africa. Data from Nigeria showed

increasing incidence since its onset with 2.98 million people currently living with HIV/AIDS and national prevalence of 4.6% [6]. The Nigerian national demographic health survey of 2013 revealed that 93-96% of Nigerians aged 15-49 years were aware of HIV/AIDS. It noted some reduced knowledge among rural dwellers, the uneducated and that the women from the South-South region of the country were among those more likely to have multiple sex partners. A researcher reported poverty, illiteracy, economic-driven-migration activities and unemployment as some of the socioeconomic risk factors for vulnerability of women to clandestine risky sexual exposure to HIV/AIDS [7]. There were conflicting reports of effects of educational attainment [8] and socio-economic status [9] on HIV from some parts of sub-Saharan Africa and suggestions that the partner's socio-economic status measured by education or income/employment may be a stronger predictor of female HIV serostatus than measures of female socio-economic status [9].

Consistent use of condom and limiting sexual intercourse to one uninfected partner evidently reduce the risk of heterosexual transmission. Evidence revealed too that positive behavior changes tend to alter the course of epidemic while stigma and discrimination, lack of access to services and bad laws worsen the epidemic [5]. Treatment, prevention, care and support

are the key responses to people living with HIV/AIDS.

In Sub-Saharan Africa more women than men are living with HIV/AIDS. More than half of HIV-positive adults in the region are females [10] making the African women the most vulnerable and worst hit by the pandemic. In this region, women aged 15-24 years are 8 times more likely than men to be HIV positive [5]. According to the 2003 data about half of them are aged 15-24 years

The relative increase vulnerability of women include their increased physiological susceptibility and gender inequalities like increased vulnerability to rape, sex with older men, unequal access to education, socioeconomic and political opportunities, violence and fear of violence [5, 11]. Young women mostly in sub-Saharan Africa therefore have lower level of accurate and comprehensive HIV knowledge than men of their age [11]. They are less likely to report use of condom in sex [11] as they have little capacity to negotiate safer sex [5,12], access the services they need and utilize the opportunities for empowerment [5]. This is because women especially in low and middle income countries face significant barriers to accessing services due to economic constraints and gender related discriminations [11].

According to WHO some 3.34 million children globally are currently living with HIV/AIDS and most of them were due to vertical transmission

from their HIV-positive mothers during pregnancy, labor or breastfeeding [4]. More than 700 children are newly infected daily [4]. Since heterosexual contact followed by mother to child transmission remain the leading means of HIV transmission, then deeper understanding of the epidemiological factors in women will ensure more effective planning, implementation and monitoring of prevention and control strategies of HIV/AIDS. The objective of this study is to determine the socio-demographic and bio-clinical characteristics of women who were HIV seropositive in pregnancy. It is hoped that data from this study will add to the already existing pool of evidence in furthering the concerted efforts at combating the HIV/AIDS scourge.

SUBJECTS AND METHODS:

ST Philomena Catholic Hospital (SPCH) was selected as the site for this project. SPCH is located at the center of Benin City in Edo state in South-south region of Nigeria. Benin City is the capital of Edo state which has an estimated population of over 4 million with about 1.2 million residents in Benin City. SPCH is a 120 bedded secondary tier mission health facility with over 70 years' obstetric services to the communities in and outside Edo state. It also offers laboratory and pediatrics services including prevention of mother to child transmission (PMTCT) of HIV/AIDS program. There are about a thousand deliveries annually. The records of pregnant women that

attended SPCH were retrospectively reviewed for the HIV positive mothers that had their delivery between 2009 and 2013.

For each mother that tested positive to HIV the next two mothers that tested negative were recruited to serve as the control. The files were traced from the Labor ward records and retrieved with the assistance of the medical records staff. Relevant data on sociodemographic and bio-clinical variables were extracted into the computer using a designed proforma. For the purpose of this study, the main sociodemographic variables were maternal age, parity, occupation, educational attainment, marital status and social class; while the bio-clinical variables included prenatal care attendance, booking and last prenatal weight, booking and last prenatal haematocrit, neonatal birth weight, preterm labor and delivery, Apgar score at 5 minutes and perinatal deaths. All the files of those who declined HIV testing and incompletely documented files were excluded from the analysis.

The social classification was based on the educational attainment of the women and the occupation of their husbands [13]. The husband occupation was classified into professionals, middle level and unskilled with allocated scores of 1, 2 and 3 respectively. The education of the women was scored 0, 1 and 2 respectively for university, secondary and

primary levels of education. The aggregate of the two scores was the social class.

For the purpose of this study the social class I and II was the upper class, class III middle class while IV and V formed the lower class. Unmarried referred to state of being single, separated, divorced or widowed at the time of delivery. Unbooked referred to a pregnant woman that never had the benefit of prenatal care at the facility before presentation in labor irrespective of her doing so elsewhere.

Preterm labor or delivery was labor or childbirth before 37 completed weeks of gestation; stillbirth was intrauterine fetal death any time after 24 weeks of gestation while perinatal death was stillbirth or neonatal death within the first seven days of birth. Parity was the number of previous childbirths to neonates alive or dead after 24 completed weeks of gestation. Maternal age was the age of the woman in completed years at the day of her childbirth. Women who were in government paid employment were classified as civil servants; those employed in private organization were classified as private employees while those in their private business were classified as self-employed. Those training for job or studying in educational institution were students and those not in any paid job (self or private organization or government) were classified as housewives. The center collaborates with other organizations in HIV/AIDS prevention and control programs in the country. The study was

approved by SPCH research and ethics committee.

Statistical analyses were with EPI INFO Version 3.5.1 and INSTAT software. Statistical testing was done with Chi square (X^2) and Fisher's exact test, while means were compared by Student t-test with $P < 0.05$ considered as statistical significance.

RESULTS:

One hundred and sixteen 116 (2.94%) of the 3951 women who had their child birth at SPCH within the period of this study tested positive to HIV testing. The age range of the 116 women in the study group was 19-43 years, mean age of 29.7 ± 4.6 years; for the 232 women in the control group the corresponding values were 19-40 years and 29.3 ± 4.6 years. The difference in mean age between the two groups was not statistically significant ($P = 0.45$). The women in age range of 25-29 years statistically significant tested less positive to HIV infection in pregnancy (OR 0.61, $P = 0.04$) while those aged 30-34 years were about 90% increased HIV seropositive in pregnancy (OR 1.91, $P = 0.01$). There was no statistical significant linear relationship between the age of the women and HIV infection during pregnancy ($X^2 = 0.7283$, $P = 0.39$).

Educational attainment has a significant inverse association with the odds of HIV seropositivity in pregnancy ($P = 0.01$). The

mothers with primary and secondary levels of education from table 1 had increased odds of being infected with the former worse and significantly infected (OR=2.2, $P = 0.048$). Those without formal education were too few for comment. From Table 1, there was significantly reduced HIV seropositivity among the married mothers (OR 0.1212, $P = 0.0441$). The women who were unbooked for prenatal care but presented in labor were twice HIV positive relative to their booked counterparts. The difference however was not statistically significant (OR: 1.99; $P = 0.098$). The nulliparous women were 20% at increased odds of being HIV positive (OR: 1.19, $P = 0.4919$). The parous ones were some 10% less likely to test HIV positive in pregnancy. The differences were not statistically significant.

There was some 40% reduced prevalence of HIV infection among the women from the upper social class and increase of similar magnitude among those from the lower class (OR=1.43, $P = 0.15$). The differences were not statistical significant. Occupation of the women appeared to have significant influence on HIV seropositivity in pregnancy.

The data in Table 1 showed that the civil servant mothers were statistically significant about 50% less HIV seropositive in pregnancy (OR=0.5141, $P = 0.049$). The women employed in the private organization and those self-employed were 40% and 50% respectively associated with increase HIV seropositivity in

pregnancy. The differences however, were not statistically significant. The students were 30% less HIV infected in pregnancy (OR: 0.6719, P: 0.3152) but the difference was not statistically significant.

From Table 2, significantly more than twice of the HIV-positive women were anemic at commencement of prenatal care (OR=2.13, P=0.0023). The study group had a significant lower mean booking haematocrit (P=0.0015) which later became similar to that of the control group at term. Both the study group and the control group were similar in mean booking weight (P=0.31) but the study group weighed significantly less at term relative to the control counterparts (P=0.0013). The study group had relatively more antepartum hemorrhage though the difference was not statistically significant. Again, the study group ruptured their fetal membranes more frequently than the control group but the difference was not statistically significant. (OR=1.34, P=0.44).

The study group twice as their control counterparts had preterm births (OR=2.016, P=0.059) and newborns with Apgar score of <7 at 5 minutes (OR=2.12, P=0.11) though the differences were not statistically significant. The mean weight of the newborns of the study group was 0.20kg less than the control group (P=0.0032). Their neonates were significantly more than 7 times likely to suffer intrauterine growth restriction (OR=7.19, P=0.0002) and more than thrice to be low birth weight

(OR=3.23, P=0.0017). The fetuses of the study group were twice as likely as those of the control group to suffer intrauterine death (IUD) (OR=2.07, P=0.18) and perinatal death (OR=2.08, P=0.13) respectively. These differences were not statistically significant.

DISCUSSION:

The prevalence of HIV in pregnancy in this study was 2.94% which was lower than the national prevalence of 4.6%. The prenatal seroprevalence in Nigeria has stabilized from 4.4%-4.1% from 2005 to 2010 [18]. The report also noted the variation in prevalence among the states and sites [18]. Another report from Benin City was 5.2% [14], and other South-south regional reports ranged 3.5-10.9% [15-19]. Reports from other regions of Nigeria were 5.4-8.6% from South East [18, 20, 21], 0.7-5.1% from South West [18, 22], 2.0-5.8% from North East [18, 23], 2.2-12.7% from North central [18,19, 24] and 1.0-5.1% from North West [18].

Literature from other sub-Saharan African countries reported HIV sero-prevalence in pregnancy of 6.9 -8.7% in Tanzania [25-26], 30.0% in Blantyre Malawi [27]. A national prevalence of 0.45% was reported in USA [27] while zero HIV seroprevalence was reported among Afghanistan obstetric women [29] and 0.19% prevalence among over 500 female sex workers [30].

Table1: Socio-demographic Characteristics by HIV Status

Variables		HIV-Positive n=116 (%)	HIV-negative n=232 (%)	OR	95% Confidence interval	P-value
Maternal age(years)	≤19	1(0.9)	2(0.9)	1.0	0.09-11.15	1.0
	20-24	15(12.9)	30(12.9)	1.0	0.51-1.94	1.0
	25-29	37(31.9)	101(43.5)	0.61	0.38-0.97	0.04*
	30-34	47(40.5)	61(26.3)	1.91	1.19-3.06	0.01*
	≥35	16(14.9)	38(16.4)	0.82	0.43-1.54	0.64
Educational attainment	nil	1(0.9)	1(0.43)			
	Primary	16(13.8)	16(6.9)	2.16	1.038-4.49	0.048*
	Secondary	47(40.5)	84(36.2)	1.20	0.76-1.90	0.48
	Tertiary	52(44.8)	131(56.5)	0.63	0.40-1.0	0.053
Marital status	Married	112(96.6)	231(99.6)	0.12	0.013-1.1	0.0441*
	Unmarried	4(3.4)	1(0.4)			
Parity	0	54(46.6)	98(42.2)	1.191	0.76-1.87	0.4919
	1-4	61 (56.6)	129 (55.6)	0.8856	0.57-1.39	0.6481
	≥5	1(0.9)	5(2.2)			
Occupation	Civil servant	15(12.9)	52 (22.4)	0.5141	0.28-0.96	0.0429*
	Private- organization	7 (6.0)	9 (3.9)	1.591	0.58-4.39	0.4182
	Self- employed	66 (56.9)	108 (46.5)	1.516	0.97-2.38	0.0876
	Housewife	16 (13.8)	29 (12.5)	1.120	0.58-2.16	0.7370
	Students	12 (10.4)	34 (14.7)	0.6719	0.33-1.35	0.3152
Social class	Upper	27(23.3)	76(32.7)	0.62	0.37-1.04	0.08
	Middle	43(37.1)	83(35.8)	1.06	0.67-1.68	0.81
	Lower	46(39.6)	73(31.5)	1.43	0.90-2.28	0.15
Booking status	Booked	102(87.9)	217(93.5)	0.50	0.23-1.08	0.098
	Unbooked	14(12.1)	15(6.5)	1.99	0.92-4.27	0.098

*Indicates significant

Table 2: HIV status of women by Bio-clinical Variables

Bio-clinical Variables		Subjects		OR (95% Confidence Interval(CI))	t-test	P-value
		HIV-Positive N=116 (%)	HIV-negative N=232 (%)			
Maternal outcome variables	Anemia at booking	55(53.9)	76(35.5)	2.13 (1.32-3.43)		0.0023*
	Anemia at term	34(37.0)	50(25.8)	1.69 (0.99-2.87)		0.070
	Mean booking wt (kg)	71.92±13.85	73.69±14.62	-	1.024 (-1.63 to 5.17)	0.31
	Mean wt at term (kg)	76.60±13.21	80.70±13.91	-	2.49 (0.86-7.34)	0.013*
	Mean booking PCV	32.04±3.74	33.45±3.62	-	3.20 (0.54-2.28)	0.0015*
	Mean PCV at term	34.12±4.22	35.03±4.56	-	1.61 (-0.20-2.02)	0.11
	Antepartum hemorrhage(APH)	5 (4.3)	7 (3.0)	1.45 (0.45-4.67)	-	0.54
	Postpartum hemorrhage(PPH)	2 (1.7)	12 (5.2)	0.32 (0.071-1.46)	-	0.15
	Premature rupture of membranes	13 (11.2)	20 (8.6)	1.34 (0.64-2.80)		0.44
	Preterm labor/delivery	17 (15.7)	19 (8.5)	2.016 (1.001-4.057)		0.059
Perinatal outcome variables	Apgar score <7at5 min	12 (10.3)	12 (5.2)	2.12 (0.92-4.87)		0.11
	IUGR	13 (11.6)	4 (1.7)	7.19 (2.29-22.60)		0.0002*
	Mean birth weight (Kg)	3.064±0.683	3.260±0.521		2.97 (66.07-326.35)	0.0032*
	Low birth weight	20 (17.4)	14 (6.0)	3.23 (1.59-6.27)	-	0.0017*
	Stillbirth	8 (6.9)	8 (3.4)	2.07 (0.76-5.68)		0.18
	Perinatal mortality	9 (7.8)	9 (3.9)	2.08 (0.80-5.40)		0.13

*Indicates significant,

The wide national, regional and global variations in HIV sero-prevalence is possibly a reflection of differences in the level of awareness about HIV/AIDS, sexual behavior, socio-cultural and religious practices and not racial or biological differences.

From our results, there was a lack of linear relationship of HIV infection in pregnancy by age. However contrary to global reports that majority of HIV positive women were of young age group of 15-24 years [5] the most affected in this study were aged 30-34 years. This compared favorably with a Nigerian nationwide survey report [18] and in contrast to another report from Niger Delta region of Nigeria [15]

Our data did not include the timing of the age at the contraction of the virus by the affected women. Again the pregnant women were a subset of the heterogeneous women population varying in age, parity and other characteristics coupled with the fact that HIV infection is a chronic disorder therefore our results may have been confounded by these factors. A well structured longitudinal study will define better the most vulnerable age group as it is more likely to time the age at seroconversion of each victim. If HIV prevalence among the pregnant women aged 15-24 years is used as a proxy for measuring rates of new infection in a population [15, 19], then our results appeared to suggest stabilizing or declining new infections. There was an evidence of consistent decline in HIV prevalence among young

women aged 15-24 years [18]. With the increasing access and use of antiretroviral therapy and the anticipated increase survival of victims, increasing proportion of older seropositive women would be expected as suggested by our results.

The women of low parity (nullipara and primipara) appeared to be at increased vulnerability to HIV seropositivity in pregnancy. This compared with reports from other researchers [15], [18]. Wide bio-social gap seemed to be a risk factor in this group. The increased seropositivity among the nullipara and primiparous women appeared to suggest increased premarital infection especially for the nulliparous women and the possibility of combined premarital and marital infection for the primiparous ones. Our data suggested an inverse relationship of education on HIV infection contrary to report from other authors [15, 28]. Low educational attainment has been associated with reduced knowledge about HIV/AIDS and this has been reported as a possible socioeconomic risk factor for HIV infection [6, 7]. Our results suggested that the more educated women were less affected as reported by other authors [18, 31]. Evidence suggest that they may have adopted HIV/AIDS risk reducing behaviors more readily than the less educated as they were more privileged to be more exposed to health promoting information or more empowered to negotiate protective sexual behaviors with their sex

partners [31-32]. Evidently, HIV prevalence fell more consistently among highly educated groups than among less educated groups, in whom it was reported that HIV prevalence sometimes rose while overall population prevalence was falling [8]. More recent data suggest that greater HIV risk in the more educated at earlier period of the epidemic was giving way to more HIV risk reduction [8].

The women who presented for the first time in labor (unbooked) were twice as likely to be seropositive as their booked counterparts. Over a quarter of a cohort of unbooked obstetric women were reported HIV seropositive in a previous study in this region [34]. It was reasonable to assume that some seropositive women that were aware of their status out of the fear of stigmatization and discrimination may hide their status by either withdrawing from prenatal course, decline testing, or change their health facility only to be detected lately on presentation in labor or other pregnancy complications. It has been reported that the concerns regarding the possibility of stigma and discrimination, abuse and violence could deter women from seeking HIV testing or other essential health services [11]. The implication of this finding is to double the efforts to empathetically manage all unbooked obstetric patients as they present mostly in labor. This is expected to optimize maternal health and prevent mother to child transmission of HIV, an important route of its spread, by ensuring prompt HIV testing, antiretroviral

therapy and other PMTCT interventions. The possibility of poverty [27] and lack of support as the reason for the failure of some of them to access prenatal care could not be ruled out too since some of the study group were unmarried, poorly educated and unemployed.

From our results, occupation of the mothers appeared to influence the odds of contracting HIV infection. Those who were gainfully employed especially the civil servants appeared less vulnerable to the infection. This was comparable to one other report [6] but contrasted with another [15]. The socioeconomic status did not strongly influence the acquisition of HIV infection from our results. A further analysis for linear tendency failed to strongly suggest this. This compared with evidence from other parts of Africa [31, 35, 36]. There was an increased incidence of anemia among the HIV positive mothers similar to other reports [1-3]. There has been a report of association of HIV infection and anemia [2]. Anaemia in this group is possibly from direct viral effect, bone marrow suppression from released cytokines and chronic inflammation from opportunistic infections and poor dietary intake of iron rich haematinics [2]. Again the setting is in malaria endemic zone and this possibly increased the susceptibility of the study group to malaria attack and consequent anemia [2]. They improved at term suggesting that quality prenatal interventions can ameliorate their anemic state. There was reduced weight gain in pregnancy among the

HIV-positive mothers. The loss of weight gain in pregnancy has been previously reported [1]. The study group as compared with another report [1] had increased incidence of preterm labor and delivery, intrauterine growth restriction, low birth weight and intrauterine fetal death. These possibly contributed to the increased perinatal mortality as suggested from our results and comparable to another reports [37]. Though it has been reported that HIV infection has little or no effect on pregnancy outcome [1-2] especially in a population with high maternal baseline immunity, adequate prenatal care, early diagnosis and antiretroviral therapy and reduced viral load [1], the reverse is true where these are lacking or poor as in sub-Saharan region as suggested by our results. Limitations of this study include its being a retrospective study. A well designed prospective study would have been better. A multicenter data will be more generalizable relative to an hospital based study .This study was based on first prenatal visit routine HIV testing results and this excluded the possible new infections in pregnancy and sero-conversions after booking due to window period phenomenon. This could introduce under reporting of seropositive prevalence in pregnancy as evidenced by other reports [30, 38]

CONCLUSION:

The prevalence of HIV seropositivity in pregnancy was still high. Quality education and

gainful employment have significant influence on the sero-prevalence in pregnancy. HIV infection in pregnancy appeared associated with increased maternal and perinatal morbidities. Empowering women with quality education and occupation backed with sustained advocacy on HIV risk reduction will positively impact on obstetric HIV infection.

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COMPARISON OF THE HEART RATES AND BLOOD PRESSURE OF NORMOTENSIVE AND HYPERTENSIVE BETEL NUT (ARECA CATECHU) CHEWERS

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ABSTRACT:

Betel nut chewing is a common habit in Papua New Guinea. Although much is known about this habit and its link to oral cancer, there is paucity of data on its effect on the cardiovascular system. The acute effect of betel nut chewing on the heart rate and blood pressure of 44 normotensive and 10 hypertensive subjects who volunteered to participate in this study were assessed. The heart rate and blood pressure of each subject in both groups were measure before and after chewing betel nuts. The results showed statistically significant increase in the mean heart rate from baseline after two ($P=0.032$, $df=4$) and seven minutes ($P=0.024$; $df=4$) in the normotensive but not in the hypertensive subjects. The results for the blood pressure were variable in both groups. Our findings indicate that betel nut chewing acutely increases the heart rate in normotensive compared to hypertensive subjects.

Key words: betel nut, areca catechu, heart rate, blood pressure response, cardiovascular effects

Submitted: October 2014; Accepted: January 2015

INTRODUCTION

Betel nut chewing has been shown to increase the heart rate [1]. This effect lasts for 17 minutes regardless of whether the chewer is a novice or habitual chewer [1]. Although the main active compound in betel nut is thought to be arecoline, which is a naturally occurring analogue of acetylcholine, the effect observed after chewing suggest sympathetic stimulation

[2]. There are several hypotheses trying to explain the transient tachycardia in betel nut chewers. Nicotinic receptors are present on adrenal medulla [3] and it has been proposed that stimulation of these receptors may release Catecholamines causing tachycardia [4, 5]. Betel nut chewing has also been shown to increase basal secretions of catecholamines [4]. Piper betel inflorescence that is chewed

with the betel nut has also been shown to release catecholamines in-vitro [1, 6]. However, the exact mechanism explaining tachycardia observed in betel nut chewers is yet to be elucidated.

Few studies have examined the blood pressure response after chewing betel nut. Systolic blood pressure has been observed to be elevated in first time chewers but not the diastolic [1]. In an epidemiological survey, chronic chewers were found to have high prevalence of hypertension [4]. Hence, the acute and chronic effects of betel nut chewing on blood pressure are still unknown.

Betel nut quid chewing is a popular habit in Papua New Guinea (PNG). There are no published data comparing the heart rate and blood pressure among normotensive and hypertensive chewers of betel nut quid in PNG. This baseline study was prompted by the lack of such data. The major aim of this baseline study was to compare the heart rate and blood pressure of normotensive and hypertensive chewers of betel nuts. It is hoped that the results obtained in this study will set the stage for detailed study to assess the effects of betel nut chewing on the cardiovascular system.

SUBJECTS AND METHODS:

This was partly a hospital based cross-sectional study. The study sites were the Port Moresby General Hospital (PMGH), which is the major specialist, general and referral hospital in the National Capital District and

PNG and the School of Medicine and Health Sciences (SMHS) University of Papua New Guinea (UPNG). Two study groups were used. In the first group were healthy normotensive subjects and in the second group were hypertensive patients. Convenience sampling was used to select the normotensive subjects from the SMHS UPNG and the hypertensive subjects from the hypertensive consultation clinic in PMGH.

All subjects were screened using pre-defined criteria. The exclusion criteria included - non-betel nut chewers, history of angina, history of angina on chewing betel nut, past history of ECG evidence of arrhythmia, heart block or any abnormal conduction, past history of abnormal echocardiography findings and history of allergies. All the hypertensive patients were on Propanolol, which is a beta blocking anti-hypertensive agent. The subjects were appropriately informed about the study and the option to withdraw at anytime during the course of the study.

Informed consent was obtained from 44 healthy normotensive subjects selected from the SMHS UPNG and 10 hypertensive patients from the hypertension consultation clinic in PMGH. Betel nuts, piper betel inflorescence and lime powder were purchased from local markets in Port Moresby.

Measurements of the various parameters were carried out in the Sir Buri Kidu Heart Institute located within the PMGH. Cardiac resuscitation equipment was set up and standardized

appropriately. The study protocol was explained to each subject before commencement of the procedure. Each subject was given time to acclimatize to the environment to allow the heart rate and blood pressure to reach resting levels, while sitting comfortably on a chair.

After ten minutes of rest, baseline heart rate was obtained using radial pulse and recorded as beats per minute (bpm); then blood pressure was measured using a mercury sphygmomanometer and listening for Korotkoff sounds over the left brachial artery. Korotkoff sound phase I was taken as systolic blood pressure (SBP) and phase V was recorded as diastolic blood pressure (DBP) [7]. Three separate measurements were recorded for each subject. Baseline measurements were recorded as zero time. The recordings were done by the same investigator for the entire study period to reduce any inter-observer variability.

Each subject was then given a betel nut, betel inflorescence and lime powder to chew. A hand held digital stop-watch was used for time keeping. After the subjects started chewing, heart rate and blood pressure were measured at two, seven, 12 and 17 minutes. Measurements were obtained while the subject was still sitting on a chair.

Ethical clearance and approval for the study were obtained from the Ethics and research grant committee in SMHS UPNG. The study

was done in accordance with the Declaration of Helsinki [8].

The heart rate and blood pressure measurements before and after chewing were analysed using Microsoft Excel data pack. Paired student t-test was done to assess the statistical significant of the changes in the mean heart rate and blood pressure from the baseline measurements. A $p < 0.05$ was defined as statistically significant with the null hypothesis being no change in the mean heart rate and blood pressure after chewing betel nut [9].

RESULTS:

Mean Heart rate after chewing betel nut:

In the normotensive subjects the mean heart rate increased significantly to 95 ± 18 bpm (mean \pm standard deviation) ($p = 0.032$, $df = 4$) after two minutes from the baseline (zero time) heart rate of 69 ± 11 bpm (Table 1).

The difference from baseline remained significant after seven minutes (HR=88 bpm; $p = 0.024$; $df = 4$). It then decreased gradually close to baseline level after 12.0 and 17.0 minutes. The corresponding mean heart rate at 12.0 minutes and 17.0 minutes were not different statistically compared to the mean baseline heart rate. In the hypertensive patients, the mean heart rate increased to 78 ± 11 bpm after two minutes from a mean baseline of 70 ± 12 bpm (Table 1). The difference was not statistically significant

($p=0.18$; $df=4$). The heart rate then decreased gradually after two minutes to the baseline level. Figure 1 shows the changes in the heart rate of the normotensive subjects compared to the hypertensive patients.

The significant increase in the heart rate of the normotensive subjects after two minutes was significantly different from the non-significant increase observed among the hypertensive patients.

Table 1: Mean heart rate of normotensive subjects and hypertensive patients

Time (minutes)	Mean Heart Rate of Normotensive subjects		Mean Heart Rate of Hypertensive patients	
	bpm \pm std dev (n =44)	P-value	bpm \pm std dev (n =10)	P-value
0 (baseline)	69 \pm 11		70 \pm 12	
2.0	95 \pm 18	0.032*	78 \pm 11	0.180
7.0	88 \pm 12	0.024*	77 \pm 10	0.193
12.0	83 \pm 12	0.060	74 \pm 10	0.423
17.0	77 \pm 9	0.118	71 \pm 10	0.836

*Statistically significant

Figure 1: Mean heart rate of Normotensive subjects and Hypertensive patients

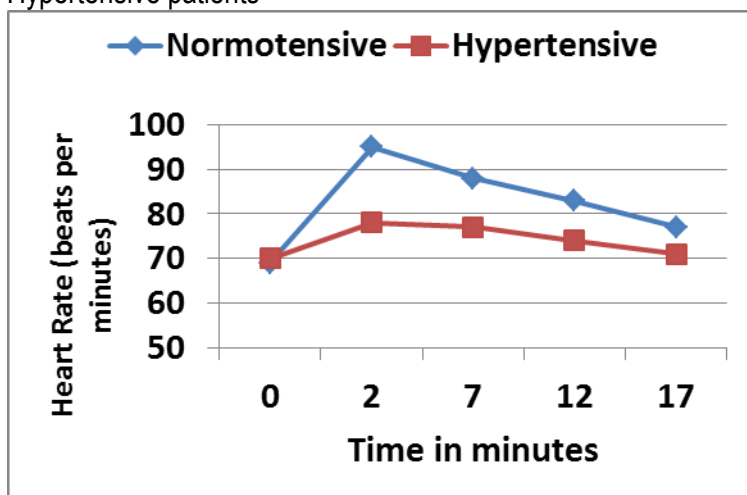


Table 2: Mean systolic (SBP) and diastolic (DBP) blood pressure of normotensive subjects and hypertensive patients.

Time (minutes)	Mean Blood Pressure of Normotensive subjects (n = 44)				Mean Blood Pressure of Hypertensive patients (n = 10)			
	Mean SBP (mmHg)	P value	Mean DBP (mmHg)	P value	Mean SBP (mmHg)	P value	Mean DBP (mmHg)	P value
0 (baseline)	117±7		80±9		146±14		90±12	
2.0	117±14	1.0	75±12	0.405	134±10	0.088	83±9	0.158
7.0	118±12	0.866	80±12	1.0	142±16	0.091	89±10	0.836
12.0	119±11	0.709	83±10	0.539	140±16	0.089	90±12	1.0

Blood pressure after chewing betel nut:

The mean systolic and diastolic blood pressure recorded for the normotensive subjects at baseline and at 2.0, 7.0 and 12.0 minutes after chewing betel nut is presented in Table 2. There were no statistically significant changes in the mean SBP from the baseline value. The mean DBP decreased slightly, from baseline, but the difference was not statistically significant ($p=0.4$; $df=4$). The mean SBP and DBP for the hypertensive patients decreased from the baseline values after two minute of chewing betel nut. The differences in both cases were not statistically significant (Table 2). The drop was transient, in each case, returning to the baseline values in subsequent readings.

DISCUSSION

Betel nut contains four alkaloids; arecoline, arecaidine, guvacoline and guvacine that may

be responsible for its pharmacological effects [10]. Current evidence suggests that arecoline may be the most active compound [3, 10]. Arecoline is an acetylcholine agonist acting on muscarinic and nicotinic receptors [3, 10]. Pharmacological effects of betel nut chewing are thought to be due to parasympathetic stimulation which includes euphoria, central nervous system stimulation, vertigo, excessive salivation, miosis and tremor [3, 10].

Physiologically acetylcholine is a neurotransmitter in the autonomic nervous system and is broken down by Acetylcholinesterase to acetate and choline [3, 10, 11]. An iso-enzyme of Acetylcholinesterase, called Pseudocholinesterase, is in plasma or serum where it is used to monitor cholinesterase-inhibiting properties of pesticides and toxicity among agricultural workers [11, 12]. Data from in-vitro studies

suggest arecoline may be broken down by Pseudocholinesterase and Carboxylesterase [13].

We observed a statistically significant increase in the mean heart rate two minutes after chewing betel nut in the normotensive subjects. This increase was transient and may have been induced through stimulation of the sympathetic nervous system. Nicotinic receptors are present on adrenal medulla [3] and stimulation of nicotinic receptors by arecoline may release catecholamines into the circulation thus causing tachycardia [4, 6]. Betel nut chewing has been reported to increase basal secretion of catecholamines from adrenal chromaffin cells and in low doses stimulates the sympathetic system [4]. Chu [1, 2] reported that there was rise in the heart rate lasting 16.8 minutes in betel nut chewers regardless of whether they are chronic, occasional or novices, and that only the systolic blood pressure was increased. Our results support these findings although the increase in heart rate among the hypertensive patients was not statistically significant, which may have been caused by beta blockers; all the hypertensive patients in our study were on Propranolol, a beta blocking anti-hypertensive agent. No statistically significant changes were observed in the SBP and DBP in our study. Acetylcholine has been shown to cause vasodilation in vessels with intact endothelium [12, 15, 16]. Arecoline may also be a peripheral

vasodilator, albeit less potent than acetylcholine, which may explain the trend towards hypotension observed in the present study. More studies are needed to explain these changes in blood pressure among betel nut chewers. Epidemiological data from studies in the Asian population suggest a link between hypertension and habitual betel nut chewing [1, 4]. This may be a chronic effect rather than acute. Further, addition of spices to betel nut for chewing as practiced in most Asian countries may be a contributing factor towards development of high blood pressure in habitual betel nut chewers [1, 4].

In our study the observed mean heart rate changes from baseline were transient. This may possibly due to rapid metabolism of arecoline by Pseudocholinesterase, a similar mechanism as for acetylcholine, although the role of Pseudocholinesterase in arecoline metabolism is unclear [12]. The acute transient tachycardia may be a risk factor for cardiac arrhythmias in predisposed patients [17, 18]. Betel nut chewing has also been implicated in acute myocardial ischaemia [19, 20], these earlier observations are now supported by epidemiological data showing association between betel nut chewing and cardiovascular death [5, 21, 22, 23, 24].

In the presence of lime, arecoline is hydrolyzed to arecaidine which has sympathetic effects via inhibition of Gamma-Aminobutyric Acid (GABA)

uptake [25]. Piper betel inflorescence has been shown to release catecholamines in-vitro [6, 25] which may also explain the tachycardia in betel nut chewers. There is no clear scientific evidence to indicate if the sympathetic effects of betel nut chewing have direct cause-effect relationship to clinical or sub-clinical ischaemic heart disease. The results obtained in this study strongly indicate the need for detailed study to assess the effects of betel nut chewing on the cardiovascular system of chewers in Papua New Guinea.

CONCLUSIONS:

Betel nut chewing has effect on the cardiovascular system. The acute effects appear to be transient increase in the mean resting heart rate noted two minutes after chewing and returned to baseline readings after 15 minutes. The exact mechanisms for the increase in resting heart rate after chewing betel nut are yet to be confirmed by detailed studies. There is no change in blood pressure.

Study limitations:

The sample size of the hypertensive patients was very small because of the difficulty in getting such volunteers to participate in research studies. The subjects were not separated according to gender.

This study excluded occasional and novice betel nut chewers. The results from our study should be interpreted as preliminary data,

which should serve as baseline for more detailed multidisciplinary study.

ACKNOWLEDGEMENTS

We acknowledge the board of directors of Sir Buri Kidu Heart Institute for financial support and approving this research to be carried out at the institute.

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EFFECT OF BLOOD TRANSFUSIONS AND NON -TRANSFUSION ON SERUM FERRITIN LEVELS OF PATIENTS WITH SICKLE CELL DISEASE ATTENDING THE PAEDIATRIC HAEMATOLOGY CLINIC OF THE UNIVERSITY OF BENIN TEACHING HOSPITAL

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ABSTRACT:

The need for recurrent blood transfusion is thought to be protective against iron deficiency in children affected by sickle cell disease. However, the subject has not received sufficient attention in Nigeria. The objective of the study was to assess the iron status of transfused and non transfused sickle cell disease children aged 1-18 years who are in steady state, using serum ferritin levels. In this cross-sectional study, 100 children with sickle cell disease aged 1-18years attending the Paediatric Haematology Out-Patient Clinic were recruited consecutively. The subjects were in steady state and had not received blood transfusion in the last 3 months. Their iron status was determined using serum ferritin levels. Serum ferritin levels of <25ng/ml was used to establish the presence of low iron stores. A patient with low mean corpuscular volume for age together with low serum ferritin (<25ng/ml) was considered to have iron deficiency anemia (IDA). Fifty four (54%) of the 100 subjects had received blood transfusion. The lowest mean serum ferritin value of 34 ± 36.1 ng/ml was seen amongst subjects who had never received blood transfusion in the past. The prevalence of iron deficiency was 35.2% and 60.1% in transfused and non transfused SCD children respectively. The prevalence rates of iron deficiency anemia (IDA) were 14.8% and 30.4% respectively in transfused and non transfused SCD children. The prevalence of iron deficiency increased with the duration of blood transfusion. 20.8% of those who had received blood transfusion less than a year prior to the study were iron deficient while 85.7% of those who received blood more than 5 years prior to the study were deficient. This difference was statistically significant. Iron deficiency and iron deficiency anemia were seen in transfused and non transfused SCD children but the prevalence was higher in the non-transfused group. Transfusion given more than 5 years ago, was not protective against the presence of iron deficiency.

Key words: Sickle cell disease, children, serum ferritin, iron deficiency, iron deficiency anemia

Submitted: February 2015; Accepted March 2015

INTRODUCTION:

Sickle cell disease (SCD) is the commonest haemoglobinopathy in Nigeria with prevalence as high as 3% in the newborn population [1]. The disease is associated with chronic haemolysis resulting in anemia [2]. Other haematologic complication of the disease like aplastic anemia, hyper-haemolysis (usually following infections) and sequestration crisis often worsen the anemia resulting in the need for blood transfusion [2,3,4]. In a study of 131 SCD children aged 9months to 15 years in Western Nigeria, 43.5% had received blood transfusion and 57% of those transfused had had multiple transfusions [5]. In the management of certain complications of SCD like stroke, priapism, and acute chest syndrome, repeated blood transfusions are usually advocated [6]. As a consequence, SCD children are highly predisposed to the need for recurrent blood transfusions. Transfusions should protect the SCD child from developing iron deficiency anemia as each unit of blood delivers 200 g of iron to the recipient [7].

One major complication that may arise from frequent transfusions is iron overload. The diagnosis of iron deficiency or overload is based largely on laboratory assessment [8,9]. The routine blood investigations done in most health facilities is not able to detect iron

overload and may only suggest the presence of iron deficiency. This is because mean corpuscular volume (MCV) is 97% specific for the diagnosis of iron deficiency [9]. Various studies [9, 10] have shown a good correlation between serum iron and body iron stores even amongst SCD patients. This is because serum iron levels are roughly proportional to total iron stores. In a study carried out by Vichinsky et al [9] involving the use of several forms of tests to determine iron status in SCD patients, serum ferritin measurement <25ng/ml was most specific for iron deficiency. In that study, there were no false positive results with the use of this method. In Nigeria, most health facilities lack the laboratory facilities required for routine assessment of iron status in these children. The above reason prompted the present study.

The main purpose of our study is to assess the iron status of transfused and non-transfused SCD children using their serum ferritin levels as criteria. Other objectives of the study were to describe the frequency of blood transfusion and the effect of interval of blood transfusion on iron status.

PATIENTS AND METHODS:

This cross-sectional study was conducted between May and June 2009. One hundred SCD children attending the Consultant Out

Patient Clinic (Paediatric Haematology) of the University of Benin Teaching Hospital were studied. The subjects were aged 1-18 years, and were in steady state of health. A patient is said to be in steady state if he/she is afebrile, and free of complications at the time of sampling. Patients who had received blood transfusion in the last 3 months prior to the study were excluded. Five millilitres of blood was collected by venepuncture. Haemoglobin concentration (Hb), packed cell volume (PCV), and mean corpuscular volume (MCV) were assessed using the Abacus junior model automated analyser [11], reticulocyte counts were done using microscopic viewing after staining with brilliant cresyl blue solution and serum ferritin was done using the Ferritin Quantative Test Kit (a solid phase enzyme-linked immunosorbent assay) with the optic density of each sample determined by the Chemware microtitre reader (Awareness Technology USA 2006 Model).

A subject was classified as iron deficient (reduced iron stores) if the serum ferritin is <25ng/ml, and those with co-existing low MCV for age (0.5-2years<70fl, 2-5yrs <73fl, 5-9yrs<75fl, 9-14yrs<76fl, 14-18<77fl) [12] were classified as having iron deficiency anemia (IDA). Patients with serum ferritin levels higher than normal for age were classified as having iron overload.

Ethical approval was obtained from the Ethic and Research Committee of the University of Benin Teaching Hospital. Informed consent was obtained from the patients and /or their parents/caregivers.

The data obtained was analysed using the statistical package for Social Sciences (SPSS) software package version 13.

Values were expressed as means and standard deviation. The student's T-test was used to compare means and Chi square was used to compare proportions. Fisher's exact test was used to compare frequencies when the cell value was less than 5.

RESULTS:

A total of 100 SCD children age 1-18 years in steady state were recruited into this study. They were made up of 60 males and 40 females. The mean age of all the children was 7.7 ± 4.8 years with a median of 6.5 years. Ninety seven (97%) of them were haemoglobin (Hb) SS whilst the remaining 3 (3%) were HbSC.

Fifty four (54%) of these children had received blood transfusion. Of these, 18 (33.3%), 15 (27.8%), and 21 (38.9%) had received one, two or more than 3 transfusions respectively in the past.

Haematological parameters of transfused and non transfused subjects:

Table 1 shows the haematological parameters of the transfused and non-transfused subjects. The serum ferritin level was higher in the transfused than non transfused subjects but this difference was not significant. There was no statistical significant difference in the other parameters above between the transfused than non transfused subjects. Of the 54 patients who had been transfused, 19 (35.2%) had low serum ferritin. Of these, 11(20.4%) had serum ferritin levels less than 25ng/ml (iron deficiency) but had normal MCV, while 8 (14.8%) had low serum ferritin and low MCV for age showing the presence of IDA. None of 54 transfused patients had levels above normal for age. While of the 46 who had never been transfused, 28 (60.3%) had serum ferritin less than 25ng/dl. Of these, 14 (30.4%) had iron deficiency (low serum ferritin only) while 14 (30.4%) had IDA (low serum ferritin and low MCV for age). None had iron overload.

The prevalence of iron deficiency (reduced iron stores) in the transfused and non transfused patients was therefore (19/54) 35.2% and (28/46) 60.9% respectively (Table 2). This difference was statistically significant ($p=0.016$, OR =1.7).The prevalence of IDA was (8/54) 14.8% and (14/46)30.4% in the transfused and non transfused patients respectively. The lowest mean serum ferritin value of

34 ± 36.1 ng/ml was seen among subjects who had never been transfused. The mean serum ferritin level was higher in patients with 2 transfusions than patients with ≥ 3 transfusions (Table 3). The difference in the mean serum ferritin levels in the subjects who had never been transfused and those who had received one, two and three or more transfusions was not statistically significant ($p=0.31$).

Number of blood transfusions and iron status of the study population:

Iron deficiency was highest (60.9%) in subjects who had not received any previous blood transfusion (Table 4).

Interval since last blood transfusion and iron status of the subjects:

There was a statistically significant association between the period preceding the last blood transfusion and the presence or absence of iron deficiency ($p=0.002$).

The prevalence of iron deficiency increased as the time interval between the last blood transfusion and the study period increased. Five (20.8%) of twenty four subjects who had been transfused in the last one year were iron deficient while six (85.7%) of the seven subjects who had been transfused for more than five years preceding the study iron deficient (Table 5).

Table 1: Hematologic parameters of transfused and non transfused subjects

Laboratory parameters	Previous Transfusion		t	p-value
	Yes (Mean±SD)	No (Mean±SD)		
Packed Cell Volume (%)	22.3±3.2	23.2±3.8	1.29	0.20
Mean Corpuscular Volume (fL)	77.9±9.3	74.9±8.5	1.70	0.10
Haemoglobin concentration (g/dl)	7.4±1.1	7.6±1.2	0.87	0.39
Reticulocyte count (%)	2.5±1.5	2.6±1.4	0.34	0.73
Serum Ferritin (ng/ml)	46.9±35.2	34.0±36.1	1.85	0.07

Table 2: Iron status in transfused and non-transfused subjects

Iron Status	Previous blood transfusion	
	Yes: n = 54 (%)	No: n = 46 (%)
Deficiency	19 (35.2)	28 (60.9)
Normal	35 (64.8)	18 (39.1)
Overload	0	0

p=0.016; OR = 1.7

Table 3: The mean serum ferritin levels according to the number of previous blood transfusions

No of previous transfusions	No of subjects	Mean serum ferritin (ng/ml)
None	46	34.0±36.1
Once	18	43.5±39.6
Twice	15	52.1±34.9
≥three times	21	46.0±33.0

p = 0.31

Table 4: Number of previous blood transfusions and the iron status of study subjects

No of blood transfusions	Iron status		Total N(%)
	Deficient n (%)	Normal n (%)	
None	28(60.9)	18 (39.1)	46(100)
Once	8(44.4)	10 (55.6)	18(100)
Twice	4(26.7)	11(73.3)	15(100)
≥ Three times	7(33.3)	14 (66.7)	21(100)

$$\chi^2 = 7.7, df=3, p=0.05$$

Table 5: Comparison of interval between last blood transfusion and iron status

Time interval α (years)	IRON STATUS			p-value	OR
	Deficiency N(%)	Normal N(%)	Total N(%)		
<1	5(20.8)	19(79.2)	24(100)	0.08	0.5
1 – 2	3(25.0)	9(75.0)	12(100)	0.51	0.7
3 – 4	5(45.5)	6(54.5)	11(100)	0.49	1.4
>5	6(85.7)	1(14.3)	7 (100)	0.006	3.1

$$\chi^2=11.1, df=3, p=0.001 \quad \alpha = \text{interval between last transfusion and time of study}$$

DISCUSSION:

Blood transfusion was common among our patients with SCD. This is not surprising as similar finding has been reported from a previous study in Nigeria [5]. In two separate studies in Senegal, of the 323 SCD children

aged 5months to 22 years and 60 SCD patients studied, 30% and 30.7% respectively had received blood transfusion [13,14]. In 186 Congolese SCD subjects aged 1-21 years, 80.6% had been transfused [15]. In Yemen, in a study of 75 HbSS patients aged 1-30 years,

41.3% had been transfused [16], while 54.3% of the 70 SCD patients aged 1-30 in the US had been transfused [9]. In Jamaica, in a study of 311 subjects, 70.6% had received at least one transfusion by the age of 20 years [17]. In another study in Brazil on 135 SCD children less than 2 years old, 12.6% had been transfused [18]. The prevalence is much lower in the Brazilian study because of the younger age of the children studied. Exposure to blood transfusion is thus a common occurrence globally although the indication for this may vary from country to country based on the preferred pattern for treatment of the various forms of crisis in SCD children and the availability of blood for transfusion.

In this study, the haematologic parameters were similar in the transfused and non transfused SCD patients. Vichinsky et al [9] noted a significant difference in the MCV level of the transfused and non transfused children. The transfused HbSS had higher MCV compared to the non-transfused HbSS patients and the mean Hb concentration was higher in the transfused group compared to the non-transfused group although it was not stated how often and how recent before the study these patients were transfused.

Iron deficiency is a spectrum; the earliest stage is depletion of iron stores which is characterized by low serum ferritin levels. The most severe form is the iron deficiency anemia (IDA) and is

characterized by low MCV and low serum ferritin levels. The prevalence of iron deficiency anemia (IDA) in the transfused and non transfused group in this study was 14.8% and 30.4% respectively. This is much higher than the 1.7% in Senegalese SCD children [14] and the 5.9% and 19.5% in the transfused and non transfused SCD children in Brazil [18] and the 3.2% and 20.5% in transfused and non transfused Yemen SCD patients [16].

In Jamaica, the prevalence of iron deficiency anemia was 8.5% amongst transfused SCD subjects [19], while in the USA, prevalence of iron deficiency in transfused and non transfused patients was 0% and (6/38) 15.8% respectively with an overall prevalence of 9% [9]. The prevalence of iron deficiency was higher in this study compared to that of the above countries. The reason for this cannot be readily explained as countries like Senegal, Brazil and Yemen are developing countries like Nigeria. In USA and probably in Jamaica, one may speculate that the children have better nutrition and probably a higher transfusion rate per individual although this was not so stated in any of the above studies.

As was seen in this study, interval of blood transfusion prior to the study period significantly affected the iron status as patients who had not been transfused for more than 5 years had significantly higher prevalence of iron deficiency compared to those who received

blood less than one year prior to the study. This further buttresses the fact that previous transfusion especially after a long interval is not protective against iron deficiency in SCD children. Iron overload was not seen in any of the subjects studied suggesting that the frequency of blood transfusion in these children was not high enough to predispose them to iron overload. Also, it suggests that the caregiver of these patients were not erroneously giving them blood tonic in an attempt to raise their PCV. This is reassuring as this practice would have been detrimental to the wellbeing of the patients. However, what appeared to be prevalent was iron deficiency in both the transfused and non transfused subjects.

CONCLUSION:

Although blood transfusion occurs commonly in SCD children, this practice is not protective against the occurrence of iron deficiency especially when the last blood transfusion is more than 5 years ago. Iron deficiency was highly prevalent among our SCD children studied.

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PROSTHETIC REHABILITATION OF THE MAXILLOFACIAL DEFECT WITH AURICULAR PROSTHESIS: A CASE REPORT

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ABSTRACT:

Losing of an ear can be a fatal experience for a patient. The deformed appearance of the face resulting after an oncosurgery or an accidental trauma may results in psychological as well as social embarrassment for the patient. It is a challenge to manage such defect on the face with surgery/artificial prostheses. Prosthetic rehabilitation of auricular defects can be a demanding procedure due to a broad variety of clinical presentations and a wide array of treatment options. The defect can be restored with custom made auricular prosthesis made up of silicon elastomeric material, which gives life-like appearance and also improves the quality of life of the patient. The patient can feel more comfortable and accepted in the social circle. A multidisciplinary approach and team management are essential in providing more accurate and effective rehabilitation of such defects. This article describes an easy technique of using silicone auricular prosthesis, with thin flash extending around the defect for better retention and orientation. Moreover it is more aesthetically acceptable and economically cost effective and such prosthesis helps patients who refuse to undergo second surgery for implant supported prosthesis.

Key words: Accidental Trauma, Loss of Ear, Silicon Prosthesis

Submitted: November 2014; Accepted: February 2015

INTRODUCTION:

Rehabilitation of the patients with acquired or congenital deformity of the head and neck region is a most challenging task that requires team approach and multidisciplinary management [1, 8]. The psychological trauma associated with such facial deformity would be unacceptable for the patient. Additionally, it also affects patient's personal, professional and social life. Rehabilitation of such defects may not only provide such individuals with professional and social acceptance but, also improves their quality of life [3] An auricular defect can be caused by several conditions including accidental trauma, congenital malformation, or surgical excision of ear in cancerous conditions. Acquired auricular deformities most commonly result from a wide range of defects associated with accidental/traumatic injuries in certain clinical cases defects caused due to human bite constitutes major cause of such maxillofacial defects [4, 5].

The rehabilitation of lost/severed ear is a major challenge for the head and neck surgeon or plastic surgeon to reconstruct due to the unique anatomical structure of the auricle that exactly resembles the contra lateral ear. Surgical reconstruction of such defects often requires

skillful surgical procedures with time span requiring several months to years. Total excision of ear hampers retention and stability factor of the prosthesis, such type of cases can be managed by implant supported prosthesis [4] and/or adhesive retained auricular prosthesis that can be considered in patients who are not willing to undergo second surgical procedure. Implant retained prosthesis may not be a treatment of choice for all cases because some patients who have underwent oncosurgery along with radiotherapy are not good candidates for implants; in such a condition prosthesis that are supported with spectacles, hair bands, and/or adhesives as a mode of retention is required [6, 9]. This article emphasizes the use of an anatomico-mechanical retentive mechanism with the use of silicone auricular prosthesis.

CASE REPORT:

A 36-year-old male patient was referred to the Department of Maxillofacial Prosthodontics, with a missing right ear. The patient was involved in a road traffic accident, which resulted in almost complete amputation of his right ear. On examination, the patient's right ear was missing (Fig. 1). There was no injury or deformity to the left ear. Different treatment options including cosmetic surgical intervention, implant retained

[2] and adhesive retained prosthesis was discussed with the patient. Patient refused any of the surgical interventions the only treatment option present was retention and stability of prosthesis that can be obtained with adhesives and anatomico-mechanical mode of retention. Thus, it was planned for prosthetic replacement of the missing ear with retentive stud of silicon prosthesis extending into the external auditory meatus. The impression of defective and the non-defective side was made with irreversible hydrocolloid impression material (Fig. 2) [1].

Before making an impression, orientation lines were marked on the face, one line bisecting the middle of the tragus vertically and the other line drawn from the ala to the middle of tragus horizontally. These lines helped in proper orientation of the wax pattern on the cast (Fig. 3). A small piece of cotton, impregnated with petrolatum was used to block the external auditory canal and an alginate impression of defective side and external auditory canal was made. The impressions were washed and disinfected with 2% gluteraldehyde solution, which were later poured with die stone to obtain

the casts. The wax pattern was fabricated over the cast with stud extension, which engages the undercut in the external auditory canal (Fig.4).

Wax pattern was fabricated onto the working cast (Donars technique) [3] the orientation, shape of the ear was exactly matched. During the trial, the position, shape and size of the wax pattern was evaluated and when found satisfactory, it was flaked using triple stage technique (Fig 5). After dewaxing, medical grade RTV silicone (cosmosil) [1] was painted into the cavity of the 3-piece stone mold as a thin semitransparent glaze to simulate superficial vasculature, pigmentation, and surface irregularities. A more opaque base color silicone mixture was then poured to fill the rest of the mold and was allowed to polymerize at room temperature [5].

Finally, the ear prosthesis was recovered from the 3-piece stone mold, trimmed and finished for extrinsic coloration [7]. Subsequently a hole was made in the prosthesis through the stud to facilitate hearing. Later on, the prosthesis was retained [5] with help of adhesives and anatomico-machanical retention mode.



Figure 1. Patient's photograph

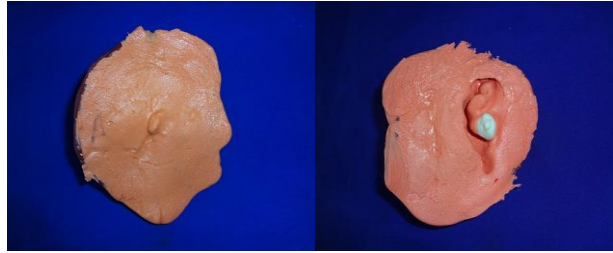


Figure 2. Diagnostic impression



Figure 3. Orientation of wax pattern on the working cast



Figure 4. orientation of wax pattern onto the defect



Figure 5. lateral, back and frontal view of the patient

Even though the prosthesis was self retentive because of the stud extending into the external auditory meatus, the spectacle frame can be used for additional retention of the prosthesis. The patient was recalled after 24 hours and was asked whether there was any discomfort or irritation to the tissues. When it was found that patient was comfortable wearing the prosthesis, regular recall check up was scheduled after an interval of 1, 3 and 6 months. At each recall, the

prosthesis was evaluated and the tissues were examined for any irritation resulting from the stud extending into the auditory meatus. It was found that the stud did not irritate the surrounding tissues or hampered the hearing capacity of the patient.

DISCUSSION:

Prosthetic rehabilitation of facial disfigurements with custom made prosthesis may improve the

level of confidence and self-esteem of the patients in the society. Difficulties with facial prosthetic devices may arise due to various reasons that mainly include depth and size of the defect, amount of soft tissue lost during surgical management, location and shape of the defect, the amount of tissue bed remaining after surgery, retentive factor of the area. Hence, the choice of rehabilitation of such defects usually depends on patient's psychological factor, as well as physical dimensions of the defect and the surface landmarks of the defect to ensure satisfactory aesthetic outcomes of the prosthesis [4].

The existing treatment modalities for replacement of missing ear are surgical management and prosthetic management. Surgical reconstruction using autologous tissue, suppose to be the most natural method of restoration of any missing part or tissue of the body. The disadvantage of surgical management is to undergo multiple surgeries over a period of time and the resulting structure may not exactly resemble the contra lateral ear to provide facial balance and to improve esthetics [4, 5]. Prosthetic replacement may provide an anatomically correct and esthetically pleasing prosthesis. The prosthetic rehabilitation of such defect includes adhesives retained, Implant retained or retention with anatomico-mechanical undercuts. Rehabilitation of facial defect with custom made silicon

prosthesis with adhesive is the most economical, conservative and a reversible type of treatment modality [5]. Implant-retained prosthesis may not be an ideal option in majority of cases due to patient's health and psychological factor; in general, patients usually do not opt for implant retained prosthesis because of financial constraints and apprehensions for surgical interventions. Also, the placement of extra oral implant depends on the thickness and amount of the bone in the mastoid region. Hence, replacement of a missing ear by surgical management with implants is not always possible or acceptable to the patient. Therefore, custom made ear prosthesis retained with adhesives and anatomico-mechanical means is a better option in some of these cases.

The most simple and easy method mentioned in this article is suitable option for such patients. Closely adapting silicon prosthesis reinforced with spectacle frame, hair band [1, 5] provides enhanced retention and orientation of the prosthesis. Stud extension into the external auditory canal and flash extension of the prosthesis in and around the defect provides reassurance of closely adapted and well retained prosthesis. The technique mentioned in the present case is mainly indicated where the patient has undergone radiotherapy and

placement of implants are relative contraindicated. The prosthesis extension into the external auditory canal may diminish hearing on the affected side to prevent this patent hole was made in the prosthesis. This procedure also reduces the problem of adaptation of prosthesis.

CONCLUSION:

This article highlights the need for the Maxillofacial Prosthodontist to adopt a flexible and open approach during treatment planning in regard to the patient's socioeconomic as well as anatomic limitations. While many retentive options are available, the adhesive retained prosthesis with stud extension into external auditory canal was considered to be the most appropriate treatment option in this case. The ultimate goal of any maxillofacial rehabilitation should be to satisfy the patient's needs and expectations while at the same time providing the best possible treatment with economically low cost rates.

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FOR THE OLD STONES IN THE DUCT; DO WE NEED A NEW GOLD STANDARD?**¹Sujatha Dyasanoor, ²Shweta Channavir Saddu, ³Beena Varma R, ³*Nidhin J. Valappila**¹Oxford Dental College, Bommanahalli, Bangalore, India²Pandit Deendayal Upadhyay Dental College, Kegaon, Solapur, Maharashtra, India³Royal Dental College, Chalissery, Palakkad, Kerala, India***Correspondence author:** nidhin.valappila@gmail.com**ABSTRACT:**

Sialolithiasis is not uncommon condition. Its historical roots can be laid back even to the writings of Oribasius. Over the years diagnostic and therapeutic modalities have changed. Currently there are many imaging modalities which can be used to detect sialolith and even 3D imaging is available. But for all practical purposes the conventional radiograph will suffice when the sialolith is in the anterior floor of the mouth.

Key words: Sialolith, sialadenitis, submandibular gland, sialolithiasis*Submitted: November 2014; Accepted: March 2015***INTRODUCTION:**

Sialolithiasis is a frequently encountered condition by dentist [1]. It finds its place even in the writings of Oribasius, who mentions it as a “calcareous concentrations in the mouth” and Alexander, a Roman physician describes it as “a stone spat by the patient from the mouth” [2]. Sometimes it may cause a diagnostic dilemma especially when it is small superficial and cause ulceration on the floor of the mouth. Variety of imaging modalities is available but old and time tested modalities are good enough

to identify and diagnose majority of the submandibular salivary calculi [3]. Availability of advanced imaging modalities is not condonable for their use especially when it involves financial burden and expendable radiation exposure to the patient.

Here we are presenting a series of case reports, some of which were diagnostic dilemma and all of which were diagnosed and managed by conventional methods.

PRESENTATION OF CASES:**CASE 1:**

A 51 years old female patient reported to outpatient department with a chief complaint of swelling in right submandibular region since 15 days. History revealed that the presence of recurrent swelling since 5-6 years which was managed symptomatically with analgesics. The pain characteristically increased during meal times only. The medical history was unremarkable. Extraoral examination revealed a palpable, firm and tender right submandibular salivary gland, while intraoral examination showed a unilateral hard swelling of right Wharton's duct with purulent discharge.

A diagnosis of chronic suppurative sialadenitis of right submandibular gland secondary to sialolithiasis was made based on the history given by the patient and the signs elicited by the clinician followed by a mandibular occlusal radiograph.

The patient was referred to oral surgery where the stone was removed by a transoral approach with a sharp dissection under local anesthesia. Antibiotics, analgesics and sialagogues were prescribed postoperatively and she was instructed to sip water regularly, application of moist heat and massage the gland to avoid recurrence. The stone measured about 9 mm in length. Subsequent follow up showed uneventful healing. (Figure 1)

CASE 2:

A male patient aged 40 years reported with complaint of pain in left submandibular region since 3 days. Patient gave history of recurrent swelling since 1 year which subsided on symptomatic management by local doctor. However from past 3 days patient was experiencing similar swelling which aggravated on eating/swallowing and subsided during rest of the day. Examination revealed palpable, non-tender swelling in left submandibular region extra orally whereas a diffuse, hard intraoral swelling was seen in left floor of the mouth. Overlying mucosa was smooth and erythematous. The left Wharton's duct opening was inflamed with pus discharge on bimanual palpation. A diagnosis of chronic suppurative sialadenitis of left submandibular gland secondary to sialolithiasis was made. Occlusal radiograph showed an oval shaped homogenous radiopaque mass measuring about 15mm x 10 mm in the left floor of the mouth. The patient was managed similarly as in case 1 and postsurgical instructions were given to avoid recurrence. (Figure 2)

CASE 3:

A male patient of 45 years of age reported with a chief complaint of pain in left floor of the mouth and difficulty in swallowing since 10 days. The pain was intermittent, dull aching which got worse during meal time and also a white mass under the tongue in the floor of mouth since three days. On examination a

diffuse, firm and tender swelling was detected in the left submandibular gland region with a white tooth like structure protruding through the mucosa in posterior floor of the mouth intraorally. Salivary flow was clear. Based on history and examination provisional diagnosis of sialo-oral fistula secondary to submandibular sialolithiasis was given. Lateral oblique view of left mandibular body and OPG (Orthopantomogram) revealed well defined oval shaped homogenous radiopacity measuring about 22mm x 12mm in relation to periapex of 38 extending to the inferior cortex of mandible. The stone was removed surgically with uneventful healing recorded in regular follow up. (Figure 3)

CASE 4:

A 32 year old male patient reported in our department with a chief complaint of ulcer and pain in floor of mouth since 2 weeks. Pain increased while having food. Patient had already consulted a dentist for the same problem and it was diagnosed as non-healing ulcer and patient was under treatment for ulcer. Failure to obtain any improvement in the condition after the treatment was the reason for the patient to visit our department. Intraorally there was a tender ulcer at the ductal opening

with pus discharge from the duct. Mandibular occlusal radiograph was taken which revealed homogenous radiopaque mass in right side of film which was diagnosed as sialolith. The salivary gland stone was removed surgically and healing was uneventful in follow up. (Figure 4)

DISCUSSION:

According to the literature sialolithiasis is one of the commonest of all non-neoplastic salivary gland disorders [1]. The incidence is about 1.0 % globally and age of occurrence ranges from 40 to 60 years, which is consistent with all our cases [4]. The findings in the four cases presented in this report are consistent with the available literature [1].

There is no consensus regarding the aetiology of sialolith, the suggested causes being viscosity of saliva and stasis of saliva in the duct, especially in the submandibular duct whose anatomy, composition and tortuous duct predisposes stasis [5]. The areas where the duct arcs around mylohyoid muscle and near the ductal openings are more predisposed to develop salivary stone. The starting point may be a nidus to which the above mentioned factors may act as additional contributors [6].

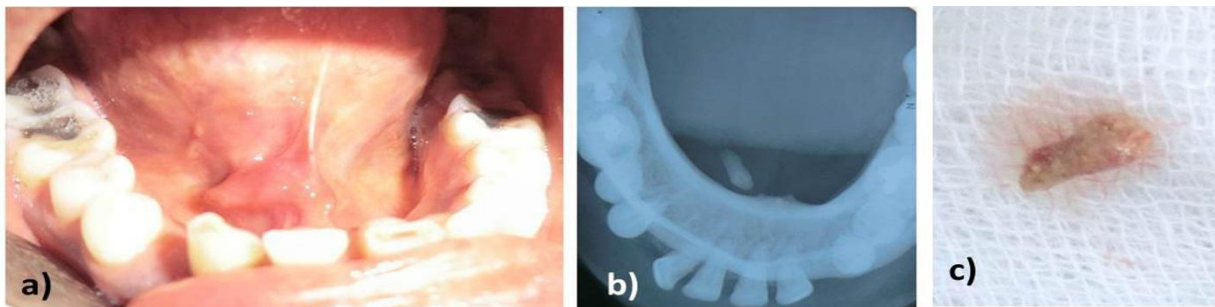


Figure 1: a) Right submandibular sialolithiasis in Wharton's duct, b) Occlusal radiograph showing typical radiographic appearance of stone in the submandibular duct, c) 9mm sialolith

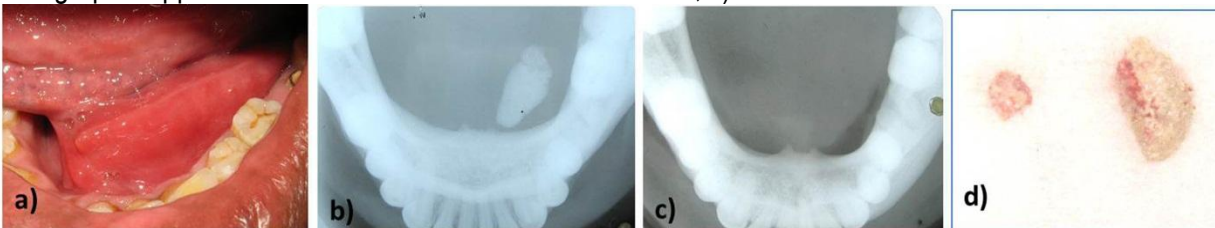


Figure 2: a) Left submandibular sialolithiasis in Wharton's duct, b) Occlusal radiograph showing radiopaque calculi in left floor of mouth, c) Sialolith measuring 15mm x 10mm, d) postoperative occlusal radiograph



Figure 3: a) Sialolith perforating through the oral mucosa, b) OPG showing radiopaque calculi superimposing over periapex of 38, c) Lateral oblique radiograph showing calculi, d) Sialolith measuring 22mm x 12mm.



Figure 4: a) Submandibular sialolithiasis in right Wharton's duct mimicking as an ulcer, b) Occlusal radiograph showing calcified stone in the submandibular duct, c) Postoperative picture showing complete healing.

The average size of the sialolith in our case series is 11.4mm ranging between 5-22mm, two of which were fairly large, one measuring about 15 mm and another around 22mm. As per

literature the average size of salivary stone is around 7mm and those more than 10 mm could be considered as unusually large [7]. In this respect two of our cases can be considered as unusually large [7].

The tendency for a sialolith to become bigger in size depends on how the disturbed duct reacts to the change. The symptoms start only when the stone grows beyond the dilating capacity of the duct and becomes symptomatic when the free flow is obstructed. When the size of sialolith increases it may cause sialooral fistula formation as was seen in Case 3.

The diagnosis of sialolith is essentially multifactorial with a thorough history, clinical examination and usage of appropriate radiographs. Reduction in salivary flow from the affected gland may be present but the classic pathognomic symptom is pain and swelling before or during meals [8]. An obstruction in the duct can cause backward flow of bacteria into the gland parenchyma causing purulent discharge from the duct, increased leucocyte count and other systemic signs [8]. Bimanual palpation in the floor of the mouth can reveal superficial stones in the Wharton's duct. More than 85% of stones in the submandibular glands are radiopaque which can be easily diagnosed using mandibular occlusal radiographs with less exposure and/or processing may reveal deep seated and even partially calcified stones [9].

Other advanced imaging modalities like ultrasonography can be considered only when the calculi are hypomineralised and not visible in conventional radiographs. Cone beam computed tomography may be good to have a 3D visualization, but other factors like increased radiation and expense to the patient

do not make it the first choice [3]. Currently digital sialography and subtraction sialography are considered to be standard procedures [10].

The treatment of sialoliths is decided by factors like size and location of stone and symptoms of the patient. For a small stone just squeezing with fingers or use of a sialagogue may be sufficient to eject it out, whereas surgical removal may be needed depending on size and location with or without antibiotics based on presence or absence of infection [11].

The latest treatment option for sialolith includes sialendoscopy which can be used for smaller size sialolith removal with minimal trauma and damage. In case of larger sized stone disintegration of stone can be done before sialendoscopy using lithotripsy. Conventional treatment modality for larger stone is open surgery with submandibular gland removal [12]. All the four cases in our present study were managed surgically and got total relief from symptoms after surgery. Post-surgical follow up and evaluation showed normal clear saliva from the ducts.

The ability to regain the normal function and flow of saliva from salivary gland depends on the position of stone in duct or inside the gland. Almost normal functioning of salivary gland can be achieved if stone is removed from the duct. The damage to the gland increases when the stone is placed inside or more proximal to the gland [13]. As there was a good recovery of the gland in all 4 cases, it made us to conclude that conservative approach as a treatment modality

should be the first consideration. Proper case selection and treatment planning play the key role in achieving good results and help in maintaining the normal functioning of the gland.

CONCLUSION:

In the present case series all four cases of submandibular sialolithiasis were diagnosed using clinical and radiographic findings and managed with no postoperative complications. As an oral physician there should be sufficient awareness about distinctive presentation of sialolithiasis which helps in early diagnosis and treatment, thus can prevent or reduces the associated morbidity. Although various advanced diagnostic aids and treatment modalities are available in the management of sialoliths, the conventional techniques still preserves their place even in the current era.

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