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Contraceptive Practices Among Women in Rural Communities in South-Western Nigeria

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Abstract – Objective : This study aims to determine the prevalence and determinants of choice of contraceptive methods among rural women in Osun state, Nigeria.
Materials and Methods : Descriptive cross-sectional, conducted among 612 women of reproductive age group, uutilising the multi-stage sampling technique.
Results : Majority of the respondents, 538(87.8%) were within the age group 20 years and above and married (86.3%). More than half 406(66.3%) were currently using a modern contraceptive method, 41(6.7%) and 4(0.7%) were using natural and traditional methods respectively, however, 161(26.3%) were not using any method, main reasons being affordability and availability 184(41.2%), and reliability (20.1%). The most significant socio-demographic determinants of ever use of contraceptives were religion and family setting, p-value 0.001 and 0.001 respectively.
Conclusion : The point prevalence rate of contraception among the rural women was 66.3%, with fear of side effect and husbands' disapproval among other reasons being the main reasons for non use.

Keywords : Prevalence; determinants; contraceptives; family planning; rural communities; reproductive age-group; women; practices; choice; methods.

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Olugbenga-Bello AI [α], Abodunrin OL [Ω], Adeomi AA [β]

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I. Introduction

Many authors raised the alarm that a stage would reach in the world when food supply would not match its population growth. (Braddocks, 1977; Huxley, 1951; Malthus, 1798; Moor, 1976) While most of the developed countries have managed to overcome this, the issue of population growth and consequent food shortage in developing countries is overwhelming. (Jones, 2004; Nwachukwu & Obasi, 2008) This expansive population growth rate has been attributed to some factors, the major of which is low contraceptive usage. (Bongaarts, 1978; Bongaarts, 1982; Osheba, 1992) In industrialized countries, virtually all married women resort to contraception at some time in their reproductive period. In contrast, the proportion reporting such use in developing countries is extremely low. (Henry & Piotrow, 1979; Khalil, Atta, Kamel & Youssef, 1996; Morris L et al, 1981).

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Nigeria which has a pop n of 140 million and an annual growth rate of 3.2 % (NPC, 2007) is the most populous country in Africa. Nigeria, according to Khurfeld (2006), is already facing a population explosion with the resultant effect that food production cannot match the growing population. In Nigeria today, the birth rates are higher than the world averages. (Nwachukwu & Obasi, 2008) Contraceptive Prevalence Rate (CPR) is still embarrassingly low in Nigeria, according to the report released by the International women's health coalition, the CPR among married women aged 15-49 years was 8% for modern methods and 12% for all methods. Also, other studies have reported a similarly low adoption rate of Modern Birth Control Methods (MBCM). (Haub & Yangishila, 1992; Makinwa-Adebusuyi, 2001; Population Reference Bureau, 2002; UNFPA, 2007).

Like many other developing nations, majority of Nigeria's population (about 70%) live in the rural communities. (Ekong, 2003) These rural communities have very high fertility rate and the CPR is also considerably lower in rural areas with CPR of 8% as compared with 18% in the urban areas in Nigeria. (Ekong, 2003;) Many rural women are reportedly reluctant to accept any artificial method of contraception. (Gaur, Goel M.K, Goel M, 2008) Several studies also revealed that rural women who were unwilling to accept family planning methods were concerned about child survival and viewed children as a source of support in old age. (Kartikeyan & Chaturvedi, 1995).

Adopting MBCM is a very complex sociological issue in Africa, and African women draw on a complex social repertoire in making contraceptive choices. (Johnson-Hanks, 2002) Decision-making concerning fertility control is, for many people, a deeply personal and sensitive issue, often involving religious or philosophical convictions. (Burkman, 2002) Studies carried out in Nigeria have shown that lack of adequate information and ignorance are key factors militating against family planning practice in Nigeria. (Adinma & Nwosu, 1995; Moronkola, Ojediran & Amosun, 2006) The socio-economic characteristics of women, notably educational levels have been argued to explain differences in reproductive behaviour and contraceptive choices. (Anju, Vanneman & Kishor, 1995; Caldwell, 1982; Dyson & Moore, 1983; Kazi & Sathar, 2001) The perceptions and the behaviour related to reproduction have also been said to be strongly determined by

prevailing cultural and religious values. (Srikanthan & Reid, 2008).

The introduction and acceptance of MBCM are therefore crucial in controlling the population growth in have access to effective Family Planning Methods, would prevent 23 million unplanned births, 22 million abortions, 1.4 million infant deaths, 142,000 pregnancy related deaths and 505,000 children losing their mothers due to pregnancy related deaths. This research was therefore carried out to study the current status of contraceptive use and the determinants among women in rural communities in Osun State, Nigeria with a view to making necessary recommendations that would help improve utilization of family planning services.

II. Resources and Techniques

This descriptive cross sectional study was carried out in the rural communities of Osun state, Nigeria and the target population was the women of reproductive age group in these communities with an estimated population of 1,048,456.

A multi-stage sampling technique was used to select the respondents from a total of 12 rural communities from 12 local government areas in the state. Stage 1, from a sample frame of 30 local government and 1 area office, 12 local government areas were selected using simple random sampling method. In stage 2, a list of rural areas in each local government was made and one rural community selected randomly from each list. In stage 3, numbers were given to all the houses in the community, and only the houses with odd numbers were selected while in stage 4, all women of reproductive age group within the age 15-49 years, who consented, were interviewed or self administered the questionnaires. A sample size of 384 was arrived at using the Leslie Fischer's formula for population greater than 10,000, but to increase representativeness and to make up for non-response, a total of 612 pre-tested semi-structured questionnaires were administered.

There was scoring of outcome variables for the knowledge of respondents about contraception with correct answers scored 1 point and wrong answers scored 0. After adding the scores and finding the mean, respondents who scored below the mean were regarded to be having poor knowledge and those with scores up to or above the mean to be good knowledge. Similarly for attitude, using the 5 point Likert scale, with strongly agreed and agreed scoring 1 point and disagreed, strongly disagreed and I don't know scoring 0 for correctly answered questions, and vice versa for incorrectly answered questions. Scores that are up to or more than the mean were regarded as positive attitude and those below the mean as negative attitude.

The questionnaires were manually sorted out and analyzed using statistical package for social sciences (SPSS) version 15 on the computer. Appropriate cross tabulations and test statistics were applied and the p-value set at $p=<0.05$

Nigeria. (Nwachukwu & Obasi, 2008) The UNFPA(2006) has pointed out that meeting the contraceptive needs of about 201 million women around the world who do not

III. Results

More of the respondents were in the age range of 35 years and above, 179(29.2%) followed by 20 to 29 years 155(25.3%), with a mean age of 29.59 ± 8.57 years. Most of them were married 528(86.3%), Muslims 359(58.7%), and had secondary school education 310(50.7%), while trading is the major vocation, 259(42.3%) among the respondents (Table 1).

Table 1 : Socio-Demographic Characteristics of Respondents (n=612)

VARIABLE	FREQUENCY (PERCENTAGE)
Age Group (in years)	
19 and Less	74(12.1)
20 – 24	90(14.7)
25 – 29	155(25.3)
30 – 34	114(18.6)
35 and above	179(29.2)
Marital Status	
Single	77(12.6)
Married	528(86.3)
Divorced	4(0.7)
Widow	1(0.2)
Separated	2(0.3)
Religion	
Christianity	251(41.0)
Islam	359(58.7)
Traditional	2(0.3)
Occupation	
Unemployed	1(0.2)
Teaching	10(1.6)
Tailoring	76(12.4)
Farming	113(18.5)
Student	83(13.6)
Hairdressing	70(11.4)
Trading	259(42.3)
Highest level of Education	
No formal education	70(11.4)
Primary school	149(24.3)
Secondary	310(50.7)
Tertiary	83(13.6)

In table 2, some of the respondents understood contraception to mean prevention of unwanted pregnancy 297(48.5%) and limiting the family size 199(32.5%), their source of information was mainly the health personnel, 322(52.6%). Majority of the women, 548(89.5%) did not know any side-effect of

contraceptives and 20(3.3%) of them reported condom burst/spillage as a side-effect of condom use. Two hundred and twenty nine (37.4%) respondents felt the husband should solely decide on family planning, while 131(21.4%) felt it was the wife/partner, but 252 (41.2%) felt it is a joint responsibility of husband and wife/partner.

Table 2 : Knowledge of Respondents about Contraception (n=612)

VARIABLE	FREQUENCY (PERCENTAGE)
Definition of contraception	
Prevention of unwanted pregnancy	297(48.5)
Child spacing	99(16.2)
Limit family size	199(32.5)
Prevent sexually transmitted diseases	17(2.8)
Sources of Information	
Friends / Relatives	124(20.3)
Health personnel	322(52.6)
Printed medial (postal, hand bill)	26(4.2)
Electric media (Radio, TV)	140(22.9)
Knowledge of Side-effects	
None	548(89.5)
Weight gain	8(1.3)
Weight loss	5(0.8)
Condom burst / spillage	20(3.3)
Extra marital affairs	7(1.1)
Amenorrhea	6(1.0)
Secondary infertility	6(1.0)
Heavy menses	3(0.5)
Dislodgement	5(0.8)
Irregular menses	4(0.7)
Decider of Family Planning Method	
Husband	229(37.4)
Wife	131(21.4)
Both	252(41.2)

In table 3 below, Rings 359(58.7%), abstinence 527(86.1%), male condom 571(93.3%) and injectables 491(80.2%) were the most well-known traditional, natural, barrier and hormonal methods respectively. After the scoring of outcome variables, table 4, majority of the respondents 464(75.8%) had good knowledge while the others 148 (24.2%) had poor knowledge. (table 4)

Table 3 : Knowledge about Contraceptive Methods (Multiple Response; n = 612)

VARIABLES	FREQUENCY (PERCENTAGE)
Traditional	
Armlet	178 (29.1)
Ring	359(58.7)
Pad lock	224(36.6)
Waist band	218(35.6)
Natural	
Periodic Abstinence	527(86.1)
Rhythm	344(56.2)
Lactational amenorrhoea	287(46.9)
Coitus interruptus	336(54.9)
Barrier	
Male condom	571(93.3)
Female condom	3(0.5)
Diaphragm	180(29.4)
Hormonal	
Injectable	491(80.2)
IUCD	365(59.6)
Implants	184(30.1)
Pills	485(79.2)
Surgical	
Vasectomy	2(0.3)
Bilateral tubal ligation	0(0)

Table 4 : Knowledge and Attitude of Respondents about Contraceptives (n=612)

VARIABLE	FREQUENCY	PERCENTAGE
Knowledge		
Poor	148	24.2%
Good	464	75.8%
Attitude		
Poor	86	14.0%
Good	526	86.0%

On the attitude of the respondents towards contraception, most of them strongly agreed to the national policy of 4 children per family 487(79.6%) and the involvement of husbands in family planning decisions 476(77.7%). Most of the respondents strongly disagreed with the fact that contraception was against culture and religion 382(62.4%), and that only females should use contraceptives 411(67.1%). Furthermore, they strongly disagree that contraceptives are ineffective 376(61.4%) and that it is only for the literates 489(79.9%). Appreciable number however felt contraceptives would encourage promiscuity 186(30.4%) and would diminish sexual pleasure 162(26.4%). Though 329(53.7%) and 368(60.2%) respectively felt otherwise. (Table 5)

Table 5 : Attitude of Respondents towards Contraception (n=612)

Variable	Frequency (Percentage)				
	Strongly Agree	Agree	I don't know	Disagree	Strongly Disagree
It is against culture and religion	11(1.8)	33(5.4)	161(26.3)	25(4.1)	382(62.4)
Only females should use contraceptives	34(5.6)	33(5.4)	80(13.1)	54(8.8)	411(67.1)
Contraceptives are ineffective	13(2.1)	28(4.6)	80(13.1)	175(18.8)	376(61.4)
It encourages promiscuity	96(15.7)	90(14.7)	97(15.8)	189(3.1)	140(22.8)
Diminishes sexual pleasure	51(8.3)	111(18.1)	82(13.4)	167(27.4)	201(32.8)
It is only for the literate	21(3.40)	16(2.60)	67(10.9)	19(3.2)	489(79.9)
Husbands should be involved in familyplanning decision	476(77.7)	49(8.0)	33(5.4)	36(6.0)	18(2.9)
Support national policy of 4 children per family	487(79.6)	110(17.9)	6(1.0)	5(0.8)	4(0.7)

In table 6, majority of the respondents 406 (66.3%) were currently using a modern contraceptive method, 41(6.7%) were using natural methods, 4(0.7%) were using traditional methods and 161(26.3%) were not using any method. The main reason given for choice of contraceptive methods was affordability and availability, 184 (41.2%), followed by reliability by 20.1% of the respondents. Most of the non-users 142(86.4%) did not have any reason for not using any method. Most of the users had used the method of choice between 1- 5 Years (44%), followed by 6-10 years by 26.6% of the respondents.

Table 6 : Prevalence of Contraceptive usage

VARIABLE	FREQUENCY(PERCENTAGE)
Currently used contraceptive methods (n = 612)	
None	161(26.3)
Natural	41(6.7)
Traditional	4(0.7)
Modern methods	406(66.3)
Main Reasons for choice of Contraceptive Methods (n = 447)	
No reason	98(21.9)
Affordable and available	184(41.2)
Little or no side effect	75(16.8)
Suitable effective / reliable	90(20.1)
Main Reason for not using any method (n = 165)	
No reason	142(86.4)
Side effect	13(2.6)
Husband's disapproval	6(6.2)
Desire for more children	4(4.7)
Duration of Contraceptive use(in years)(n=467)	
1 – 5	205(44.0)
6 – 10	124(26.6)
11 – 15	107(22.9)
16 – 20	28(5.9)
21 – 25	3(0.7)

Table 7 shows that the significant socio-demographic determinants of ever use of contraceptives was religion and family setting, p-value 0.001 and 0.001 respectively, but no significant associations between age, marital status, tribe and educational status with ever used family planning methods.

Table 7 : Association between Socio-Demographic Characteristics of Respondents and Ever Used Family Planning Methods.

Socio-Demographic Characteristics	Ever Used Family Planning Methods		Total (%)	Chi square	df	p-value
	No (%)	Yes (%)				
Age Group (Years)						
19 and less	18(24.3)	56(75.7)	74(100.0)			
20 – 24	24(26.7)	66(73.3)	90(100.0)			
25 – 29	37(23.9)	118(76.1)	155(100.0)	0.717	4	0.949
30 – 34	25(21.9)	89(78.1)	114(100.0)			
35 and above	41(22.9)	138(77.1)	197(100.0)			
Total	**145(23.7)**	**467(76.3)**	**612(100.0)**			
Marital Status						
Single	17(22.1)	60(77.9)	77(100.0)			
Married	128(23.9)	407(76.1)	535(100.0)	11.264	6	60.753
Total	**161(26.3)**	**451(73.7)**	**612(100.0)**			
Religion						
Christianity	45(17.9)	206(82.1)	251(100.0)			
Islam	98(27.3)	261(72.7)	359(100.0)	13.636	2	0.001
Traditional	2(100.0)	0(0.0)	2(100.0)			
Total	**145(23.7)**	**467(76.3)**	**612(100.0)**			
Family Setting						
Monogamy	71(19.7)	290(80.3)	361(100.0)			
Polygamy	57(32.8)	117(67.2)	174(100.0)	11.52	2	0.001
Total	**128(23.9)**	**407(76.1)**	**535(100.0)**			
Educational Status						
No formal education	20(28.6)	50(71.4)	70(100.0)			
Primary School	32(21.5)	117(78.5)	149(100.0)			
Secondary School	74(23.9)	236(76.1)	310(100.0)	1.361	3	0.715
Tertiary	19(22.9)	64(77.1)	83(100.0)			
Total	**145(23.7)**	**467(76.3)**	**612(100.0)**			

IV. Discussion

The awareness about contraceptive methods was generally high among the respondents with about 9 in 10 respondents knowing male condoms and 8 in 10 knowing injectables as methods of contraception and almost all of them being aware of one method or the other. This high level of awareness has been similarly reported by previous studies within and outside Nigeria. (Barrett & Buckley, 2007; Ndiaye, Delaunay & Adjamagbo, 2003; Nwachukwu & Obasi, 2008; Touati, Abdelaziz, Mtiraoui & Marzouki, 2001) The knowledge of respondents about contraception/family planning was also high with about three-quarters having good knowledge of contraception. This was also corroborated by Moronkola et al (2006) in their study carried out in south western Nigeria. This pattern should be expected in light of much enlightenment that is on-going on the issue of family planning in the country. It is however still worthy of note that some contraceptive methods were very unpopular among the respondents. Only about a quarter knew about the diaphragm and implants and not up to 1% of the respondents knew about female condoms as methods of contraception. This is most likely due to the fact these methods are not readily available and are relatively more expensive than the other commoner methods like the male condoms.

The most popular contraceptive method from this study is the male condom with more than 9 in 10 respondents knowing about it. This is similarly reported by other studies. (Kalambayi, 2006; Nwachukwu & Obasi, 2008) and is probably due to the fact that it is cheap and readily available and it is much more advertised probably also because of its dual function as a means of preventing sexually transmitted infections and also as a family planning method. Unlike in other studies where the media was the predominant source of information, (Bassey, Abassattai, Asuquo, Udoma & Oyo-ita, 2005; Onwasigwe, 2001) more than half of the respondents knew about contraception through health personnel, which is similar to the finding of a study done in Pakistan by Shah, Nisar and Qadri (2008) on the

awareness and pattern of utilizing family planning services among women attending Urban Health Care Centre. This is a pointer to the importance of enhanced primary health care services in the rural communities, though the media would still need to do much more work on public enlightenment about contraception. Also, an appreciable number (20%) heard about contraceptives from friends and relatives, and this underscores the need for peer educators in ensuring correct and adequate information about contraceptives/family planning.

Most of the respondents were favourably disposed towards contraception with more than four-fifths having a positive attitude towards contraception. However about 3 in 10 respondents felt contraception encourages promiscuity. This may be due to the conservative nature of typical African societies and could be one of the complex sociological factors (Johnson-Hanks, 2002) affecting contraceptive usage in African communities. Furthermore, nearly 90% of the respondents felt the husbands should be involved in family planning decisions and this is important because man approval and decision making has been said to be very important in utilizing family planning services, (Donati, Hamam & Medda, 2000; Shah et al, 2008; Shahin & Shahin, 2003) and this further stresses the need to carry men along in family planning campaigns.

The prevalence of modern contraceptive methods usage among the respondents was 66.3% with cost and availability being the predominant reason for choice of contraceptive methods. This prevalence is higher than the findings of other studies in rural areas in Nigeria (Nwachukwu & Obasi, 2008) and other developing countries. A study by Ndiaye, Delaunay and Adjamagbo (2003) in rural Senegal reported a prevalence rate as low as 1.5% for modern contraceptives, another study among females in predominantly rural Muslim area of North India (Gaur et al, 2008) reported prevalence of 34.9% and about half were using modern family planning techniques in the study carried out among married Sudanese women. (Ibnouf, van den Borne & Maarse, 2007) This may be due to the high literacy rate among the respondents with about two-thirds having post-primary school education, because education has been said to play an important role in women's life and assist in decision-making. (Gage, 1995; Marchant, Mushi, Nathan, Mukasa, Abdullah, Lengelen, et al, 2004) There was however no significant association between the use of contraception and educational status in this study.

The unmet need for contraception was high among the respondents with about a quarter not on any contraceptive method. This corroborates the work of Westoff (2006) that reported about one in five married women of childbearing age (22%) in Africa has an unmet need for contraception, with a higher percentage among rural women. It is even more disturbing that more than 3 out of 10 of the respondents had an unmet need for modern contraception, because other methods (eg traditional method) have been associated with high failure rates. (Westoff, 2006) There is therefore a need for more work to be done to reduce the unmet need for contraception among women because reduced unmet need for contraception is an indicator of progress toward two of the United Nations Millennium Development Goals—reducing maternal mortality and reversing the spread of HIV/AIDS—and contributes directly or indirectly to achieving all eight goals. (Population Division, United Nations, 2009) Nearly 9 out of 10 respondents who did not use contraception had no reason for not using it. The reasons given by others are the fear of side effects, husbands' disapproval and the desire for more children, which is similar to what has been reported by other studies. (Donati, Hamam & Medda, 2000; Nwachukwu & Obasi, 2008; Shahin & Shahin, 2003).

The relationship between religion and family planning has been documented by previous studies and religion has been recognized as a very important determinant of contraceptive usage. (Gaur et al, 2008; Nwachukwu & Obasi, 2008; Shah, Pradhan, Reddy & Joseph, 2006) This may explain the significant association between religion and ever used family planning methods with the Christians having a higher uptake of family planning methods than the Muslims in this study. There was also a significant relationship between family setting and ever used family planning with more women in monogamous family settings using family planning methods as compared to those from polygamous family settings. This may be a reflection of the insecurity that exists among women in polygamous family settings with the women trying to outwit each other in the number of children in other to secure their positions in the family and in the will when the husband dies.

V. Conclusion and Recommendations

The use of any modern contraceptive method was high among women of child bearing age in the rural communities of Osun State, with the prevalence rate of 66.3%, and the un-met need was 26.3%. The main reasons for non- use contraceptive were the fear of side effects, husbands' disapproval and the desire for more children, with religion and family setting having a significant association with the use of modern contraceptive methods. It is therefore necessary for religious leaders to be targeted and carried along in the campaign for modern contraceptive methods. The mass media should also be encouraged to do more in public enlightenment on the benefits of modern contraceptive methods.

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Reverse Phase-High Performance Liquid Chromatography and Ultra Violet Spectrophotometric Method for the Estimation of Raltegravir Potassium in Bulk and in Tablet Dosage form

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Abstracts - A High Performance Liquid Chromatographic (method A) and Ultra Violet spectrophotometric (method B) method were developed and validated for quantitative determination of Raltegravir potassium. The different analytical performance parameters such as linearity, precision, accuracy, limit of detection (LOD), limit of Quantification (LOQ) were determined according to International Conference on Harmonization (ICH) Q2B guidelines. Reverse phase High Performance Liquid Chromatography (method A) and Ultra Violet (method B) were developed for the determination of Raltegravir potassium in bulk and pharmaceutical dosage forms. The chromatographic separation was achieved on Symmetry C18 (4.6 x 150mm, 5 µm XTerra) column using a mixture of phosphate buffer (pH 3.0): Methanol (45:55% v/v) as the mobile phase at a flow rate 0.6 mL min-1. The Ultra Violet spectrophotometric determination was performed at 219 nm. The Linearity of the calibration curves for the analyte in the desired concentration range is good (r2 = 0.999) by both High Performance Liquid Chromatography (method A) and Ultra Violet (method B) spectroscopic method. Both methods (A&B) were accurate and precise with recoveries in the range of 98-100 % and percentage relative standard deviation (RSD less than 2%). The proposed methods were highly sensitive, accurate, and precise and hence was successfully applied for the reliable quantification of Active Pharmaceutical Ingredient content in the commercial formulation.

Keywords : *Raltegravir potassium, RP-HPLC, UV Spectrophotometry, Validation, Pharmaceutical product and Quantitation.*

GJMR Classification : *NLMC Code : QV 277*

Reverse Phase – High Performance Liquid Chromatography and Ultra Violet Spectrophotometric Method for The Estimation of Raltegravir Potassium in Bulk and in Tablet Dosage form

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Abstract - A High Performance Liquid Chromatographic (method A) and Ultra Violet spectrophotometric (method B) method were developed and validated for quantitative determination of Raltegravir potassium. The different analytical performance parameters such as linearity, precision, accuracy, limit of detection (LOD), limit of Quantification (LOQ) were determined according to International Conference on Harmonization (ICH) Q2B guidelines. Reverse phase High Performance Liquid Chromatography (method A) and Ultra Violet (method B) were developed for the determination of Raltegravir potassium in bulk and pharmaceutical dosage forms. The chromatographic separation was achieved on Symmetry C18 (4.6 x 150mm, 5 µm XTerra) column using a mixture of phosphate buffer (pH 3.0): Methanol (45:55% v/v) as the mobile phase at a flow rate 0.6 mL min-1. The Ultra Violet spectrophotometric determination was performed at 219 nm. The Linearity of the calibration curves for the analyte in the desired concentration range is good (r2 = 0.999) by both High Performance Liquid Chromatography (method A) and Ultra Violet (method B) spectroscopic method. Both methods (A&B) were accurate and precise with recoveries in the range of 98-100 % and percentage relative standard deviation (RSD less than 2%). The proposed methods were highly sensitive, accurate, and precise and hence was successfully applied for the reliable quantification of Active Pharmaceutical Ingredient content in the commercial formulation.

Keywords : Raltegravir potassium, RP - HPLC, U V Spectrophotometry, Validation, Pharmaceutical product and Quantitation.

I. Introduction

Raltegravir potassium (Fig.1) is chemically N-[(4 flurophenyl)methyl]-1, 6- dihydro-5-hydroxy-1-methyl-2[1-methyl-1-[[5-methyl-1,3,4-oxadiazol-2-yl)ethyl]-6-oxo-4-pyrimidine carboxamide potassium salt [1]. Raltegravir potassium is an enzyme integrase inhibitor used for the treatment of Human Immunodeficiency Virus 1 (HIV-1) infection in treatment experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents [2]. Raltegravir potassium targets integrase, an HIV enzyme that integrates the viral genetic material into human chromosomes, a critical step in the pathogenesis of HIV. The drug is metabolised away via glucouronidation .

Literature survey revealed that several analytical methods reported for the estimation of Raltegravir potassium in human plasma. Edward P.Acosta [3] was reported the sensitive HPLC-MS-MS method for the determination of Raltegravir potassium in human plasma. This work describes an assay system that has been developed to quantify Raltegravir concentration in human plasma using a liquid-liquid extraction technique paired with HPLC separation and MS-MS detection. Decosterd L.A [4] was reported the LC tandem MS assay for the simultaneous measurement of new antiretroviral agents: Raltegravir, Maraviroc, Darunavir, Etravirine. Single step extraction from plasma is performed by protein precipitation using 600 µl of acetonitrile. Ter Heine. R [5] was reported the quantification of the HIV integrase inhibitor raltegravir and detection of its metabolites in human plasma, dried blood spots and peripheral blood mononuclear cell lysate by means of HPLC tandem mass spectrometry. Naser L.Rezk [6] was reported an accurate and precise HPLC method for the quantification of the novel HIV integrase inhibitor raltegravir in human blood plasma after solid phase extraction. This is the first published method to use simple UV technology and reliable solid phase extraction methodology for the quantification of raltegravir in human plasma. Jean-Marie Poirier [7] was reported the quantification of the HIV integrase inhibitor raltegravir in human plasma by HPLC with fluorescence detection. Jasmine A. Talameh [8] was reported the quantification of raltegravir in female genital tract secretion using HPLC with UV detection. The method included sample preparation with perchloric acid followed by solid phase extraction. Separation with RP-

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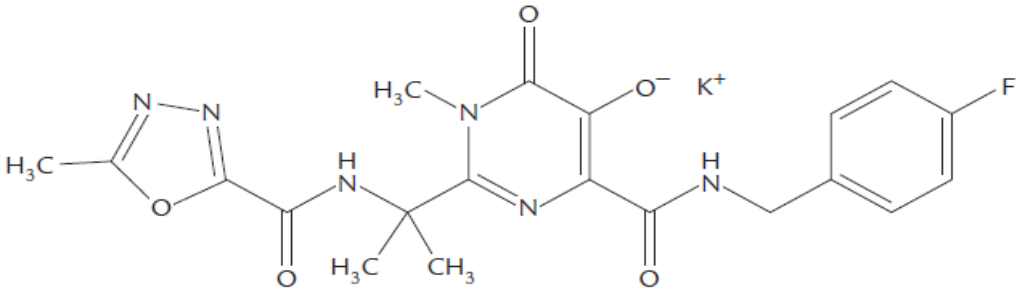

Fig. 1 : Chemical structure of Raltegravir potassium

HPLC and detection with an UV wavelength of 218 nm. Valerie Furlan [9] was reported the quantification of raltegravir in human plasma by HPLC with photodiode array detection. Notari.S [10] was reported the simultaneous determination of Maraviroc and Raltegravir in human plasma by HPLC-UV method. No methods have been reported for determination of Raltegravir potassium in bulk and tablet dosage form by RP-HPLC and UV spectrophotometric methods. The proposed research work describes the estimation of Raltegravir potassium in bulk and in tablet dosage form by RP-HPLC and UV spectrophotometric methods

II. Materials and Methods

a) Chemicals

Raltegravir potassium pure drug was received from Divis pharmaceuticals, Hyderabad. The HPLC grade Methanol, acetonitrile, water was purchased from Qualigens fine chemicals, Mumbai, India. Analytical reagent grade potassium dihydrogen phosphate and ortho phosphoric acid from Merck were used. Tablets of Raltegravir potassium 400 mg(Isentress) were procured from Merck, U.S.

b) Instrumentation and analytical conditions

Chromatography was performed using a Water series HPLC with Empower software with UV detector. Symmetry X Terra C18 Column (100 × 4.6mm, 5μ) was used. The mobile phase consists of Buffer (pH 3.0): Methanol (45:55 % v/v). The flow rate was found to be 0.6ml/min and the wavelength was found to be 218 nm. The methods were conducted using an isocratic reverse phase technique. Temperature condition was ambient. Run time was adjusted to 5min.The UV method was performed on Lab India UV spectrometer with 1cm matched quartz cells. Photo Multiplier Tube was used as detector for all absorbance measurements. Electronic balance (AFCOSET ER-200A) was used for accurate measurements and pH meter (ADWA AD 1020) was used.

c) Preparation of standard stock solution

In method [A] 10 mg of Raltegravir potassium was dissolved in 7 ml of mobile phase and made upto 10 ml with mobile phase. In method [B] 10 mg of Raltegravir potassium was dissolved in 7 ml of mobile phase and made upto 10 ml with mobile phase. Both the solution contain (1 mg/ml)

d) Preparation of sample solution (Analysis of formulation)

In method [A] twenty tablets of Raltegravir potassium containing 400 mg of Raltegravir was weighed accurately. Tablet powder equivalent to 10 mg of raltegravir potassium was transferred to a 10 ml volumetric flask, dissolve in 7 ml of mobile phase and made upto volume with mobile phase. The resulting solutions were sonicate for 10 minutes and then filter through 0.45 μm filter. Transfer 0.3 ml of the filterate into six separate 10 ml volumetric flask and made upto the volume with mobile phase (30 μg/ml). 20 μl of each solution was injected and the chromatograms were recorded. The peak area was determined and the procedure was repeated for six times. In method [B] powdered tablet equivalent to 10 mg of Raltegravir potassium was transferred to 10 ml volumetric flask dissolved and made upto the volume with solvent (1000 μg/ml). The solution was sonicate for 10 minutes and filter through 0.45 μm filter. Transfer 1ml of the filterate to 10 ml volumetric flask and made upto the volume with mobile phase (100 μg/ml). From that, pipette out 0.3 ml solution and transferred to six volumetric flasks and made upto the volume with solvent (3 μg/ml). The absorbance was measured at 219 nm. The procedure was repeated for six times.

e) Calibration graph (or) Linearity

In method [A] aliquots of stock solution of Raltegravir potassium (0.1 to 0.5 ml of 1000 μg/ml) were transferred into 10 ml standard flask and made upto the volume with mobile phase. 20 μl of the solutions were injected and the chromatograms were recorded. The calibration was done by external standard calibration. Linearity was observed between (10-50 μg/ml). In method [B] aliquots of stock solution of raltegravir potassium (0.3 to 1.5 ml of 100 μg/ml) were transferred into 10 ml standard flask and made upto the volume with the solvent (methanol and phosphate buffer pH 3.0 in the ratio 55:45 %v/v). The absorbances of the

solutions of different concentration were measured at 219 nm against blank. Linearity was observed between (3-15 µg/ml).

f) Limit of detection and Limit of quantification

The limit of detection (LOD) is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from background levels. The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with acceptable accuracy, precision, and variability. The LOD, LOQ were calculated as LOD = 3.3 σ / S and LOQ = 10 σ /S Where σ is the standard deviation of the lowest standard concentration and S is the slope of the standard curve.

g) Accuracy

The accuracy of the method was checked by recovery studies of addition of standard drug solution to pre analysed sample solution at the different concentration levels (50%, 100%, and 150%) with in the range of linearity of the drug. The results of analysis of recovery studies obtained by the method [A&B] validated by statistical evaluation.

h) Precision

Precision is the degree of repeatability at an analytical method under normal operational condition. Repeatability and intermediate precision studies were done to the precision of the method [8]. Method [A] aliquots of standard stock solution of raltegravir potassium (0.3 ml of 1000 µg/ml) was transferred into 10 ml standard flask and made upto the mark with mobile phase (30 µg/ml). 20 µl of the solution were injected and the chromatograms were recorded. The procedure was repeated for five times. Method [B] aliquots of stock standard solution of Raltegravir potassium (0.9 ml of 100 µg/ml) was transferred into 10 ml standard flask and made upto the mark with solvent (9 µg/ml). The absorbance of the resulting solution was measured at 219 nm.

i) Repeatability

Repeatability is given by interday and intraday precision. The assay and recovery procedures were repeated for three times, on the same day and once for three successive days for both the methods.

j) Ruggedness

The degree of reproducibility of the test results obtained in method [A] and method [B] of raltegravir potassium was detected by analysing the drug sample under the variety of test conditions like different analyst and different instruments is ruggedness. The procedure was repeated under the above conditions.

k) Robustness

In method [A] as a part of robustness deliberate change in flow rate (0.5, 0.6, 0.7 ml/min), mobile phase composition (10% less, actual, 10% more) was made to evaluate the impact of the method.

l) Results and Discussion

Two simple, precise and accurate HPLC and UV methods were reported for the estimation of Raltegravir in bulk and tablet formulation. Method [A], A waters HPLC system with Xterra column C18 was used for analysis. The mobile phase was optimized with phosphate buffer (3.0) and methanol (45:55 %v/v) was used for the above mentioned composition of mobile phase. Sharp peak was obtained with the retention time 4.350 minutes. The UV detection was carried out 218 nm, as Raltegravir potassium showed very good absorbance at this wavelength. An optimized chromatogram of Raltegravir potassium was shown in figure 2. The system suitability parameters like tailing factor, asymmetric factor, number of theoretical plates and capacity factors were calculated and these values were compared with the standard limit as per USP [11]. It was found that the values were within the limits (Table 1). Method [B] is a simple UV method in which the drug, Raltegravir potassium shows a absorbance at 219 nm in the solvent (methanol and phosphate buffer pH 3.0 in the ratio 55:45 %v/v). The spectrum obtained for method [B] was shown in figure 3.

m) Calibration curve (Linearity)

Raltegravir potassium was found to be obeyed Beer's law in the concentration range of 10-50 µg/ml for method [A] and 3-15 µg/ml for method [B]. The correlation coefficient for method [A] and method [B] was found to be 0.999 and 0.999 respectively. This value indicates Raltegravir potassium has a good linearity in both the methods. In method [A] calibration curve was plotted by using peak area Vs concentration. In method [B] the curve was plotted by using absorbance Vs concentration. The optical characteristics such as Beer's law limit, correlation coefficient, molar absorptivity, sandell's sensitivity, slope and intercept values for method [B] were calculated and shown in Table 2.

n) Limit of detection and limit of quantification

The limit of detection (LOD) and limit of quantification (LOQ) was calculated based on the signal to noise ratio. LOD and LOQ for Raltegravir potassium were found to be 0.027 µg/ml and 0.09 µg/ml respectively in HPLC. In UV LOD and LOQ was calculated with linearity studies. LOD and LOQ were found to be 0.0959 µg/ml and 0.290 µg/ml respectively. The results were shown in the Table 2.

o) Quantitation of formulation

The tablet formulation of Raltegravir potassium was selected for analysis and the percentage purity was found to be 100.62 % and 99.96 % for method [A] and method [B] respectively. The procedure was repeated for six times to validate the methods. The developed

methods were validated according to ICH guidelines [12]. The % RSD was found to be less than 2 %, which indicates the method [A] and method [B] had good precision. The results of analysis were shown in Table 3.

p) Accuracy

The accuracy of the method was confirmed by the recovery studies. To the pre analysed formulation a different concentration (50%, 100% and150%) of the raw material was added and the amount of drug recovered was calculated. The percentage recovery was found to be 101.6 % ± 0.2 for method [A] and 99.96 % ± 1.0692 for method [B]. The procedure was repeated for three times. The % RSD value was calculated to be 0.19 and 1.0696 for method [A] and method [B] respectively. The low % RSD value indicates that there is no interference due to excipients used in the formulation. Thus both the developed methods are found to be accurate which is shown in Table 4

q) Precision and intermediate precision

The standard Raltegravir potassium solution of 30 µg/ml was selected for analysis of method [A] and 9 µg/ml for method [B]. The % RSD value was found to be 1.44 and 0.26 respectively for precision and intermediate precision in method [A] and % RSD value was found to be 1.13 and 0.31 respectively for precision and intermediate precision in method [B]. The low % RSD value reveals that the proposed methods were precise. The results were shown in table 5.

r) Repeatability

The precision of the method was confirmed by intraday and interday analysis. The assay and recovery procedures were repeated for three times on the same day and once for three successive days for both the methods. The assay % RSD value of intraday and interday analysis of Raltegravir potassium was found to be 0.56 and 1.72 respectively for method [A]. The % RSD value was found to be 0.82 and 1.51 respectively for method [B]. The recovery studies % RSD value of intraday and interday analysis was found to be 1.04 and 2.0 respectively for method [A]. The % RSD value of intraday and interday analysis was found to be 0.65 and 1.27 respectively for method [B]. The results were shown in table 6 and 7.

s) Ruggedness

Both the methods were validated for ruggedness. The results confirmed the ruggedness of the developed method. This is shown in table 8.

t) Robustness

Robustness was performed by changing the flow rate and by changing the organic composition of phase. It shows that there is no change in the values even after making deliberate change in the analytical procedure. The results were shown in the table 9.

III. Conclusion

The HPLC and UV methods developed for Raltegravir potassium shows good precision and accuracy. The low %RSD values in the recovery studies for both the methods shows that there is no interference due to excipients and for formulation. Hence it was concluded that the developed methods are simple, precise, accurate and rapid for the analysis of Raltegravir potassium in pure and in tablet dosage form. Thus the developed methods can be adopted for the routine analysis of Raltegravir potassium in bulk and tablet dosage form.

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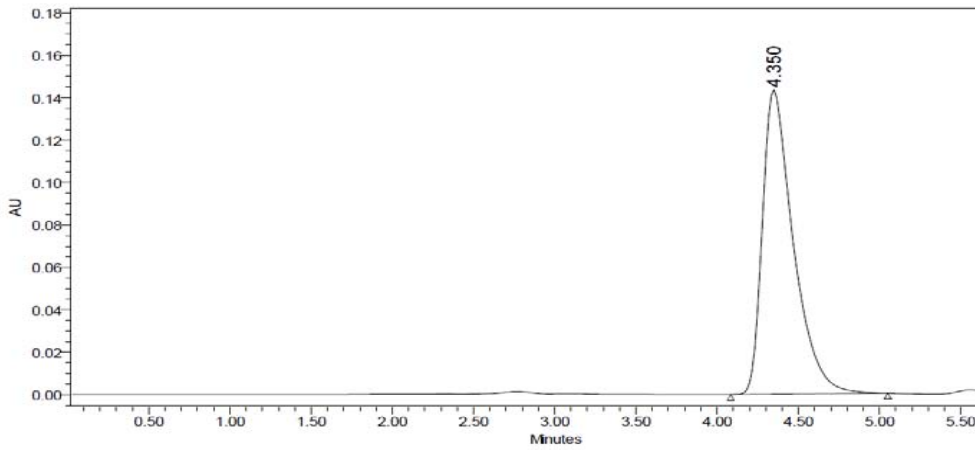

Fig. 2 : Optimized chromatogram of Raltegravir potassium

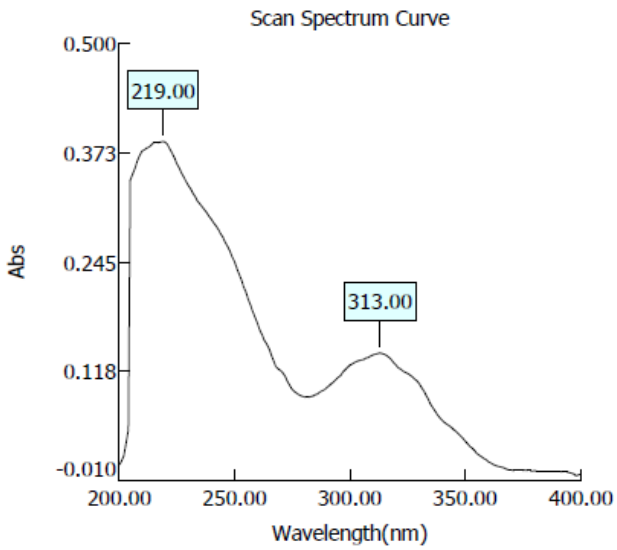

Fig. 3 : UV spectrum of Raltegravir potassium

Table 1 : System Suitability Parameters

Parameter	Experimental value	Limit as per USP
Tailing factor	1.6	Less than 2
Asymmetric factor	1.0	Less than 2
No of theoretical plates	2524	More than 2000
Capacity factor	3.5	2-10
HETP	0.059	-
Theoretical plate per unit length	16.82	-

Table 2 : Optical Characteristics of Raltegravir Potassium

Parameters	Methods	
	A (HPLC)	B (UV)
λ max`	218 nm	219 nm
Beer's law limit	10-50 μg/ml	3-15 μg/ml
Correlation coefficient (r2)	0.999	0.999
Regression equation	Y =70827x + 8620	Y= 0.0433x – 0.0024
Slope	70827	0.0433
Intercept	8620	-0.0024
LOD	0.027 μg/ml	0.0959 μg/ml
LOQ	0.09 μg/ml	0.290 μg/ml
Sandell's sensitivity	-	0.0228 μg/cm2/0.001
Molar absorptivity	-	20.6536 l/mol/cm

Table 3 : Results of Analysis of Raltegravir Potassium in Tablet Formulation

No	Amount found (mg)		% label claim		SD		% RSD	
	A (HPLC)	B (UV)	A	B	A	B	A	B
1	399.190	398.642	99.79	99.6				
2	403.285	401.604	100.8	100.40				
3	394.190	400.114	98.5	100.02				
4	395.266	399.190	98.8	99.7	1.091	0.4742	1.09	0.47
5	392.000	397.164	98.0	99.2				
6	401.020	402.000	100.25	100.50				

Table 4 : Accuracy Studies of Raltegravir Potassium

S.No.	Amount added (mg)		Amount found (mg)		% Recovery		Mean Recovery		SD		% RSD	
	A (HPLC)	B (UV)	A	B	A	B	A	B	A	B	A	B
1	5.36	5.1	5.46	5.11	101.8	100.2						
2	10.5	10.1	10.6	9.98	101.4	98.8	101.6	99.96	0.2	1.069	0.19	1.06
3	16.0	15.0	16.2	15.14	101.6	100.9						

Table 5 : Precision and Intermediate Precision of Raltegravir Potassium

Parameters	Method [A] HPLC			Method [B] UV		
	Avg. Peak Area	SD	% RSD	Avg. Absorbance	SD	% RSD
Precision	1953328	28316.4	1.44	0.369	0.0041	1.13
Intermediate Precision	2127233	5601.7	0.26	0.367	0.0011	0.31

Table 6 : Intraday And Interday Analysis Formulation

Parameters	% Estimated		% Mean		SD		% RSD	
	A (HPLC)	B (UV)	A	B	A	B	A	B
Intraday	99.94 99.91 101.13 100.22	99.04 100.03 98.21 98.42	100.3	98.92	0.570	0.816	0.56	0.82
Interday	100.66 99.51 102.50 98.45	99.86 98.27 100.54 101.92	100.28	100.14	1.733	1.516	1.72	1.51

Table 7 : Intraday and Interday Recovery Studies of Formulation

Parameters	% Estimated		% Mean		SD		% RSD	
	A (HPLC)	B (UV)	A	B	A	B	A	B
Average Intraday (50,100, 150 %)	100.84 100.81 99.01	98.72 100.02 99.41	100.22	99.38	1.047	0.650	1.04	0.65
Average Interday (50, 100, 150 %)	97.75 100.20 101.72	98.13 100.56 100.02	99.89	99.57	2.0	1.275	2.0	1.27

Table 8 : Ruggedness By Hplc And Uv Method

S.No	Type of analysis	% Estimated		SD		% RSD	
		A (HPLC)	B (UV)	A	B	A	B
1 2 3 4	Analyst-1 Analyst-2 Instrument-1 Instrument-2	99.29 100.50 98.57 97.23	99.47 97.24 101.57 98.20	1.367	1.871	1.38	1.88

Table 9 : Robustness Studies For Raltegravir Potassium By Hplc

Parameters		System Suitability	
		USP plate count	USP Tailing
Flow rate (ml/min)	0.5 0.6 0.7	2451 2669 2773	1.7 1.6 1.5
Mobile phase composition (Organic)	10% less Actual 10% more	2975 2669 2145	1.5 1.6 1.6

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HIV/AIDS Patients' Adherence To Antiretroviral Therapy In Sobi Specialist Hospital, Ilorin, Nigeria

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Abstracts - Nigeria currently accounts for about 10 percent of the global HIV burden, therefore tackling this devastating pandemic is very imperative. This study was conducted to assess the level of patients' adherence to antiretroviral therapy and identify the factors responsible for non adherence in a major HIV/AIDS specialist hospital, Sobi, Ilorin, Nigeria. Adherence among 213 HIV infected patients on highly active antiretroviral therapy was assessed using self-reporting and pill counting methods for 20 months of therapy. Structured questionnaire, personal interview and patients' hospital records were used to evaluate access to medicines and patients' factors responsible for treatment adherence. Though, the level of patients' adherence to antiretroviral drugs was low (73.3%) compared with the standard (95%), there was significant improvement compared with the earlier reported in the sub-Saharan African countries including Nigeria. Low level of education of patients, adverse antiretroviral drug effects and stigmatization were the main factors given for non adherence. Thus, Nigeria government and non-governmental organizations should intensify efforts by improving the standard of education of the citizenry, increasing the level of awareness and encouragement on HIV/AIDS status as well as continuing funding to the rural communities to stem the tide of the menace.

Keywords : *HIV/AIDS, antiretroviral drugs, adherence, counselling, patients, Nigeria.*

GJMR-K Classification : *NLMC Code : WC 503.2*

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Abstract - Nigeria currently accounts for about 10 percent of the global HIV burden, therefore tackling this devastating pandemic is very imperative. This study was conducted to assess the level of patients' adherence to antiretroviral therapy and identify the factors responsible for non adherence in a major HIV/AIDS specialist hospital, Sobi, Ilorin, Nigeria. Adherence among 213 HIV infected patients on highly active antiretroviral therapy was assessed using self-reporting and pill counting methods for 20 months of therapy. Structured questionnaire, personal interview and patients' hospital records were used to evaluate access to medicines and patients' factors responsible for treatment adherence. Though, the level of patients' adherence to antiretroviral drugs was low (73.3%) compared with the standard (95%), there was significant improvement compared with the earlier reported in the sub-Saharan African countries including Nigeria. Low level of education of patients, adverse antiretroviral drug effects and stigmatization were the main factors given for non adherence. Thus, Nigeria government and non-governmental organizations should intensify efforts by improving the standard of education of the citizenry, increasing the level of awareness and encouragement on HIV/AIDS status as well as continuing funding to the rural communities to stem the tide of the menace.

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I. Introduction

According to UNAIDS, *human Immunodeficiency Virus* (HIV) affected 30.8 million adults and 2.5 million children worldwide as at the end of 2009. Sub-Saharan Africa with just over 10% of the world's population has the greatest burden of disease (68%). In the year 2009, about 1.8 million adults and children were infected, contributing to a total of 22.5 million people living with HIV in the region. Women are particularly affected with Southern Africa accounting for about 40% of the global women living with the disease. More than 90% of the children infected are babies born to women with HIV, who acquire the virus during pregnancy, labour or delivery, or through breast milk (UNAIDS, 2010). There is therefore the need for concerted efforts toward tackling this menace. The development and widespread use of antiretroviral therapy (ART) as the treatment of choice in HIV has improved significantly the health condition of HIV positive individuals who could have untimely death. The ART however, has transformed the perception of HIV/AIDS from a fatal incurable disease to a manageable chronic illness (Palella et al., 1998). The treatment causes improvement in immunologic status and reduction in the viral load (Erb et al., 2000) which consequently reduce the incidence of hospitalization and mortality (Paterson et al., 2000).

However, incomplete medication adherence is the most important factor in treatment failure and the development of resistance. Adherence is the term used to describe the patient's behavior of taking drugs correctly in the right dose, with the right frequency and at the right time. Antiretroviral treatment success depends on sustainable high rates of adherence to medication regimen of ART (Mill et al., 2006). On the other hand, ART regimens are habitually complicated with variable dosage schedules, dietary requirements, and adverse effects (Ferguson et al., 2002). Treatment success can be precarious with missing of few doses of antiretroviral medication which leads to drug resistant strains of HIV (Bangsberg et al., 2000). An adherent patient is defined as one who takes 95% of the prescribed doses on time and in the correct way, either with or without food. Adherence is a major predictor of the survival of individuals living with HIV/AIDS (Mill et al., 2006) and poor adherence to treatment remains a major obstacle in the fight against HIV/AIDS worldwide. Low or incomplete medication adherence has been associated with detectable viral load (> 500 viral RNA copies/ ml of plasma) (Ruthbun et al., 2005) with the development of cross resistance to other antiretrovirals of the same class (Tchetgen et al., 2001). Although, more potent antiretroviral regimens can allow for effective viral suppression at moderate levels of adherence (Knafl et al 2008), none or partial adherence can lead to the development of drug-resistant strains of the virus. Cross-resistance however can potentially interfere with future therapeutic regimens for HIV-infected patients undergoing treatment and for those who subsequently become infected with resistant strains of HIV (Karl et al., 2010). The factors that influence adherence to antiretroviral therapy (ART) are in three categories viz.,

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patient-related (psychosocial and educational) factors, patient-provider factors (interaction with physicians and other health workers and access to medications) and clinical factors (pill burden, dosing frequency and adverse effects of medications) (Weiser et al., 2003).

Different levels of adherence have been reported in earlier studies in Nigeria. For instance, the levels reported for studies conducted in Kano (northern Nigeria), Sagamu, Niger Delta and Benin City (Southern Nigeria) are 49.2% (Nwauche et al., 2006), greater than 85% (Idigbe et al., 2005), 80% (Mukhtar et al., 2006) and 58% (Erah and Arute, 2008) respectively. In several countries in sub-Saharan Africa and North America, varying levels have also been reported (Mill et al., 2006). However, significant proportions of HIV-infected patients do not reach high levels of adherence and this can lead to devastating public health problems. Getting patients to take drugs everyday without failure for the rest of their lives is one of the biggest challenges. Poor knowledge of HIV/AIDS and stigmatization are also prevalent among youths affecting adherence to medication. These challenges therefore justify the necessity of continuous assessment of adherence to ART in this area. This study was therefore conducted to assess the level of adherence to ART and identify the factors responsible for non adherence in a major HIV/AIDS specialist hospital, Sobi, Ilorin, Nigeria. This study offers essential information on factors associated with antiretroviral drug adherence among adult HIV/AIDS patients.

II. Methods

a) Setting

This study was conducted at a designated HIV/AIDS treatment centre in the Sobi Specialist Hospital, Ilorin, Kwara State, located in the north central Nigeria. The hospital is a 264-bed secondary health facility with over 12 health departments offering health services to the residents of Kwara State and neighbouring States. The hospital was established by the Kwara State Government in April, 1985. The HIV/AIDS treatment centre took off in the hospital in May, 2009 with the provision of comprehensive HIV care services. As at December, 2010, 470 patients have been enrolled and 257 were receiving highly active antiretroviral therapy (HAART). The centre is currently receiving fund from a non-governmental organization (NGO), Friends for Global Health.

b) Population sample

The study sample was of 257 HIV-infected patients that enrolled and commenced HAART between May, 2009 and December, 2010. Two hundred and thirteen HIV/AIDS patients made up of 75 males and 138 females diagnosed to be living with HIV/AIDS (using both laboratory and clinical records) and on HAART treatment were selected for the study. Inclusion criteria were outpatients diagnosed and confirmed to be HIV positive, between ages of 16 and 60 years attending HIV/AIDS centre and refilling their prescription in the Pharmacy Department between May, 2009 and December, 2010. The patients were regular at the centre and using their HAART for a minimum of 6 months prior to the study. The patients also had received a fixed HAART of zidovudine(300mg), lamivudine (150mg) and nevirapine (200mg) twice daily, zidovudine(300mg), lamivudine(150mg) twice daily plus efavirenz (600mg) daily, tenofovir(300mg), emtricitabine(200mg) and efavirenz/nevirapine daily for a minimum of 6 months. The patients were consented to participate in the study. Patients excluded were children below age of 16 years and patients with history of serious cardiovascular illness, diabetes and/or cancer within the previous two years.

c) Study design

Ethical approval was sought from the management of the hospital and informed consent from all the patients participating in this study at the time of enrollment. Prior to the commencement of the study, a cross - sectional self - administered anonymous questionnaire survey was administered. Thirty patients were randomly selected and administered with a pre-tested structured questionnaire (with open-ended and/or closed questions) for the collection of socio-demographic characteristics, patients' and pharmacists' assessment of adherence and factors responsible for non-adherence among HIV/AIDS patients in the centre in order to look for flaws in the questionnaire. The questionnaire was administered twice to the 30 selected patients to ensure reliability of the data collected. The data of the 30 patients were not included in the final computation of this study. All data collected were obtained from the medical records and personal interview of the patients. The interview was carried out in local language (Yoruba language) except for 22 participants who could not understand the language and had to be interviewed in respective English and Hausa languages. The importance of the study was duly highlighted to the patients by the researcher. Learned patients themselves completed a paper format questionnaire, which was explained in details prior to completion. The 36-point questionnaire was explained before completing the questionnaire to resolve any questions regarding the questionnaire. Each of the 36-point questions was tick box format with area for writing other relevant information. The researcher also inquired other drugs taken by the patients that were not in their medical records as well as their medication-related problems. Counselling of each HIV-infected patient was usually carried out monthly at the hospital using standard procedures whenever visit is made to refill their prescriptions.

d) Adherence assessment

Self-reporting and tablet counting methods were used to determine HAART treatment medication adherence at the end of each month consecutively for eighteen months. In tablet counting, patient's medical records were reconciled against the medicines yet to be used by the patients which were brought to the pharmacy as a routine for refill of prescriptions by patients. The numbers of drug doses that the patients should have been taken but missed were also recorded. In the self-reporting of patients method, the patients were interviewed on adherence by asking them to recall how they administered drugs at home during refill of prescription. In both self-reporting and tablet counting methods, adherence was defined as taking 95% of prescribed doses over the previous month which corresponded to missing no more than one dose in a 10-day period (in a 2 times a day dosing regimen), one dose per week (in a 3 times a day regimen) or one dose per day (in a once daily dose regimen) in a 20-day period. Patients were classified as non-adherent if they missed more than 5% of their doses in at least one of the three categories or if they indicated missed doses in all three categories.

e) Statistical analysis

Data generated from the questionnaire were keyed into Genstat statistical package (Genstat, 1995) and analysed for frequencies, mean, percentages and Chi-squared test. A p-value of < 0.05 was considered significant in all statistical analysis.

III. Results

a) Socio - demographic characteristics

The Socio- demographic characteristics of the 213 patients are presented in Table 1. Out of the 257 recruited for the study, 213 met the inclusion criteria. Majority of the patients were females with 138 (64.8%), between 16 and 60 years old. The males were 75 (35.2%), some of the patients 168 (78.9%) were married, while as many as 72 (33.8%) had no formal education, but only 60 (28.1%) had primary education. The proportion of the patients with at least secondary education 81 (38.1%) is smaller compared with those without formal education. As many as 38 (36.6%) were traders and 48 (22.6%) were unemployed. The rest were 33 (15.5%) civil servants, 45 (21.1%) self employed and 9 (4.2%) students.

b) Treatment variables

In the ART clinic, the anti-retroviral drugs, opportunistic infection medicines and other palliative medications were provided free for all the HIV/AIDS patients in this setting. At the time of this study, 207 (97.2%) were on first line ART. The proportion of patients that used the different antiretroviral drug combinations were 40.9% (AZT + 3TC +NVP), 25.4% (AZT + 3TC +EFV), 2.8% (4DT + 3TC +NVP), 1.4% (4DT + 3TC + EFV), 19.7% (TDF + FTC+ EFV), 5.6% (TDF + FTC+NVP), 1.4% (ABC + 3TC + EFV) and 2.8% (AZD + 3TC + LPV/r). There were no switches from first line to second line regimen except 28% of the patients that were pregnant and were placed on second line regimen. All patients received cotrimoxazole, ferrous gluconate, folic acid, multivitamins, while some patients were on loratidine; 7.5%, amoxicillin ; 23.9%, acyclovir ; 2.3%, loperamide; 3.7%, metronidazole; 15.5%, paracetamol; 12.7%, nystatin; 3.5%; erythromycin; 7.5%, clotrimazole; 2.8%, fluconazole; 6.5%, artemether-lumefantrine; 12.7% , bromazepam; 1.4%.

c) Side effects

The most experienced effect of ARV drugs in the patients were general body weakness 38% followed by dizziness 16.4%, severe headache 14.6%, sleep disturbances 12.7% , anaemia 3.3%, vomiting 3.3%, peripheral neuropathy 1.4%, chest pain 1.4% and night micturition 1.4%(Table 2).

d) Adherence

In the present study, based on pharmacists' adherence (Table 3), 70.8% of the patients adhered strictly to their medications while patients' self-report adherence was 73.3%. The factors that could be responsible for 29.2% adherence failure (Table 4) includes medication side effects 6.6%, away from home 5.2%, illiteracy 4.7%, high pill burden 3.7%, stigmatization 3.3%, herbal medicines 2.3%, too busy 1.9%, while forgetfulness is 1.4%.

IV. Discussions

In the management of HIV/AIDS worldwide, defaulting from treatment is one of the most important problems. Cross-resistance can potentially interfere with future therapeutic regimens for HIV-infected patients undergoing treatment and for those who subsequently become infected with resistant strains of HIV (Nwauche et al., 2006). The present study showed that the youth between the ages of 16 and 40 years with mean age of 37.04 are those most vulnerable to HIV infection. This is in line with the findings of Patrick and John, (2008) that reported the majority are within the age range of 25-49 years and Chjjioke et al., (2006) with mean age of 35.04 years in Port Harcourt. In this study, women are 2 to 4 times more vulnerable to HIV infection than men during unprotected sexual intercourse because of larger surface areas exposed to contact, The female is the recipient of semen and is prone to micro trauma during sexual activity and others include early exposure to sexual activity and poverty (Van et al., 2004). In this study, the proportion of female in the treatment group is almost two-fold than that of male counterpart. This corroborates with the study of Kenneth et al., (2010)

who reported that the proportion of females was more than two-fold greater than that of the males in Benin. Contrary to this was the work of Fujie et al., (2008) in India whereby 51% of the study were male while with Thejus (2006), 69% were males. The rationale behind the high percentage of females dominates that of males especially in Nigeria is due to the fact that in many cultural believes, men are expected to have many sexual relationships. Also, women suffer gender inequalities in nature and the culture creates barriers which prevent people from taken precaution especially the women (Desilva et al., 2010). In the present study, 78.9% of the population were married which is similar to the study of Thejus, (2006) in India where 80% were married. This is expected since one of the route of HIV transmission is sexual intercourse which can easily spread among couples. This is inconsistence with work of Chijioke et al., (2006) in Portharcourt where 43% of the patients were single and 40.1% were married.

In this present study, patients on zidovudine based regimen and nevirapine based regimen were more tolerable by the patients than stavudine based therapy due to its neuropathy effect. This is inconsistent with the study of Bolton-Moore et al, (2007) that more of their patients were on stavudine based therapy compared to zidovudine regimen. In this clinical setting, the second line antiretroviral drugs were used mainly for pregnant women.The rational is to reduced as much as possible drug adverse effect on foetus,with Efavirenz being teratogenic in humans and nevirapine causes severe hepatotoxicity especially in women with CD4 count >250 cells/microliter.The adverse effects of antiretroviral drugs experienced by these patients do resolves after 2 to 8 weeks of therapy and tolerable by most of these patients(National Guideline, 2007).Some patients may required other drugs to alleviate the symptoms of medication side effects. Loratidine is used for patients with skin rash induced by nevirapine and other skin disorders. Haematinics were prescribed for these patients to improved appetite for weight gain and to prevent anaemia initiated by zidovudine. Paracetamol, amoxicillin and artemether-lumefantrine were drugs of choice for HIV patients with malaria and persistent fever. Patients need to be adviced to take efavirenz an hour after an oily food to reduce nightmares and dizziness.Very few patients experienced night micturition which may be related to zidovudine. It is advice able to screen all patients on HAART for diabetes mellitus at baseline level.

It is difficult to measure adherence in the outpatient setting with absolute precision and accuracy (Flexner, 1997). Adherence may be measured in the clinical setting in a different ways such as patient self-reports(convenient and inexpensive), clinical assessments, pill counts(labour intensive), Directly Observed Therapy on AntiRetroviral Therapy (DOTART, theoretically associated with 100% adherence, labour intensive and impractical outside institutional setting),pharmacy records/ prescription refill monitoring, biological assays(plasma drug level) and medication event monitoring system(expensive) (Cramer et al., 1998). Adherence percentage is calculated as the observed number of doses divided by the number of expected tablets taken multiplied by hundred. In this research work, pharmacists' assessment of adherence of 70.8% was quite below 95% of adherence expected of these patients but higher in comparison with the studies of Da Silvera et al., (2003) in Portharcourt with 49% and Mary et al., (2009) in India of 60% adherence levels. The present study had a better adherence rate similar to the earlier findings of Murri et al., (2001) of 74.3%. The reasons for improved adherence level in this hospital was that all the services rendered to these patients were at no cost which includes free, regular and uninterrupted supply of quality antiretroviral (ARV) drugs, medical laboratory tests and financial support. Also, drugs for opportunistic infections and palliative care were all made free for both in and out patients. Rapid improvement in symptoms and signs that brought the patients to the hospital encouraged adherence. No food restriction, proper follow up, monthly adherence counselling and high literacy level were contributing factors to adherence rate in this study. Less than one third of these patients failed to adhere to their medication schedule probably for the following reasons; medication side effects, away from home, high pill burden, illiteracy, herbal medicines, stigmatization and too busy at work/school. Medication adverse effects of antiretroviral drugs were a major barrier to drug adherence. Severe vomiting associated with zidovudine which did not resolve after 8 weeks of administration in very few patients could result to non adherence and therapeutic failure. Though in a very few patients, taking the drugs after food reduce this effect. Yellowish eyes, a pointer of liver injury may create fear for the patients to continue medication. Drug side effects as a non adherence factor is consistent with the works of Attaran et al., (2006) and Karl et al., (2010) in South Africa.

One quarter of the people living with HIV/AIDS demonstrated difficulty in comprehending simple medication instructions. Illiteracy has a disadvantage to drug adherence in this research work as supported by Kalichman et al., (2000). The higher the level of education, the better the understanding of the disease state and the comprehension of instructions given on drug usage. These could invariably enhance adherence. The minimum number of tablets to be swallowing daily by the patients throughout their lifetime is seven. The number is burdensome and disgusting for the patients to continue their medications. However, stigmatization of HIV/AIDS patients by the society contributes to non drug adherence. Some patients felt embarrassed while taking their medical folders to pharmacy for prescription refill, despite these folders were similar to other patients

in the hospital. In agreement with present study, Grierson et al., (2000), reported that HIV/AIDS patients have difficulties in taking drugs in public and carrying drugs around thereby adversely affecting adherence. The studies of Talam et al., (2008) in Kenya and Yao et al., (2010) in Togo also supported above listed factors associated with non adherence.

V. Conclusion

In Sobi specialist hospital, Ilorin, a resource poor area in Nigeria, the level of adherence to antiretroviral drugs is low compared with standard level of 95% drug adherence and this corroborates with earlier reports in Kano, Sagamu, Niger Delta, Portharcourt and Benin City in Nigeria, other African countries like Kenya, Togo and South Africa as well as India and North America. Level of education of the patients, adverse antiretroviral drug effects and stigmatization were the main factors for non adherence. Thus, Nigeria government and the NGOs should intensify their efforts by improving the standard of education of the people, increasing the level of awareness of HIV/AIDS, encourage the people to know their HIV status and continuing funding the projects to the rural communities.

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Table 1 : Socio-demographic characteristics of HIV positive patients at specialist hospital, Sobi, Ilorin, Nigeria.

Variable	Total % N= 213	Male (%) N= 75	Female (%) N= 138	P value
Age 16-30	72(33.9)	24(11.3)	48(22.6)	
31 – 40	78(36.8)	27(12.6)	51(23.9)	
41 – 50	51(24)	18(8.5)	33(15.5)	0.012
> 50	12(5.3)	6(2.8)	6(2.8)	
Marital status				
Single	21 (9.9)	6(2.8)	15(7.0)	
Married	168(78.9)	60(28.2)	108(50.7)	
Widowed	15(7.0)	6(2.8)	9(4.3)	0.052
Divorced	9(4.2)	3(1.4)	6(2.8)	
Level of education				
No formal education	72(33.7)	24(11.3)	48(22.5)	
Primary	60(28.2)	21(9.8)	39(18.3)	0.002
Secondary	51(24)	18(8.5)	33(15.5)	
Tertiary	30(14.1)	12(5.6)	18(8.5)	
Occupation				
Trader	78 (35.7)	27(12.7)	51(23.9)	
Civil servant	33(15.5)	12(5.6)	21(9.9)	0.004
Self employed	45(21.1)	15(7.0)	30(14.1)	
Student	9(4.2)	3(1.4)	6(2.8)	
Not employed	48(22.6)	18(8.5)	30(14.1)	

Table 2 : Treatment variables of HIV positive patients at the specialist hospital, Sobi, Ilorin, Nigeria.

Antiretroviral drugs combination	N (%)
AZD + 3TC +NVP	87 (40.9)
AZD + 3TC +EFV	54 (25.4)
4DT + 3TC +NVP	6 (2.8)
4DT + 3TC + EFV	3 (1.4)
TDF + FTC+ EFV	42 (19.7)
TDF + FTC+NVP	12 (5.6)
ABC + 3TC + NVP	3 (1.4)
AZT + 3TC + LPV/r	6 (2.8)
Opportunistic infection Medicines	
Loratidine	16 (7.5)
Amoxicillin	51 (23.9)
Acyclovir	5 (2.3)
Loperamide	8 (3.7)
Metronidazole	33 (15.9)
Paracetamol	27 (12.7)
Nystatin	7 (3.5)
Erythromycin	16 (7.5)
Clotimazole	6 (2.8)
Fluconazole	14 (6.5)
Artemether-Lumefantrine	27 (12.3)
Bromazepam	3 (1.4)
Medication Side effects of antiretroviral drugs	
Rashes	16 (7.5)
Sleep abnormalities	27 (12.7)
Anaemia	7 (3.3)
Chest pain	3 (1.4)
Asthenia	81 (38.0)
Headache	31 (14.6)
Dizziness	35 (16.4)
Peripheral Neuropathy	3 (1.4)
Vomiting	7 (3.3)
Night micturition	3 (1.4)

Table 3 : Patients' and pharmacists' assessment of adherence

Findings	Number of patients
Pharmacists assessment of adherence	
Adherent	151(70.9%)
Non-adherent	62(29.1%)
Self report patient assessment of adherence	
Adherent	156(73.2%)
Non-adherent	57(26.8%)

Table 4 : Factors responsible for non adherence among HIV/AIDS patients in Sobi specialist hospital

Adherence factors	Failed to take drugs as schedule	Total N =213 (%)	Males N=75 (%)	Females N=138 (%)	χ^2	P value
Away from home	Yes No	11(5.2) 202(94.8)	7(3.3) 68(31.9)	4(1.9) 134(62.9)	1.646	0.199
Too busy	Yes No	4(1.9) 209(98.1)	3(1.4) 72(33.8)	1(0.5) 137(64.3)	1.049	0.306
Forgetfulness	Yes No	3(1.4) 210(98.6)	1(0.5) 74(34.7)	2(0.9) 136(63.9)	0.852	0.386
Herbal medicine	Yes No	5(2.4) 207(97.2)	1(0.5) 74(34.7)	4(1.9) 133(62.4)	0.001	0.993
High pill burden	Yes No	8(3.8) 205(96.2)	2(0.9) 73(34.3)	6(2.8) 132(62)	0.017	0.461
Medication side effects	Yes No	14(6.6) 198(93)	5(2.3) 70(32.9)	9(4.2) 129(60.6)	0.461	0.038
Stigmatization	Yes No	7(3.3) 206(96.7)	4(1.9) 71(33.3)	3(1.4) 135(63.4)	0.156	0.156
Illiteracy	Yes No	10(4.7) 203(95.3)	3(1.4) 72(33.8)	7(33.3) 131(61.5)	0.052	0.303

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Atrioventricular Node : Presence of New Functionally and Anatomically Distinct AV Pathway

By Julia Niehues da Cruz, Daniela Delwing de Lima, Débora Delwing Dal Magro, José Geraldo Pereira da Cruz

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Abstract - The atrioventricular (AV) node is crucial to conducting electrical impulses from the atria to the ventricles in order to coordinate heart rate. This study sought to describe electrophysiologic characteristic and possible anatomic site of atrial retrograde slow AV node pathway. The role of this pathway in the initiation and maintenance of AV node reentrant in the AV block still unclear, and the possible anatomic sites of this pathway have not been reported.

Keywords : *AV node, electrocardiogram, reentry, retrograde conduction*

GJMR Classification : *NLMC Code : WG 140*

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Atrioventricular Node: Presence of New Functionally and Anatomically Distinct AV Pathway

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I Introduction

The AV node has mystified generations of investigators over the last century and continues today to be at the epicenter of debates among anatomists, experimentalists, and electrophysiologists. Historically, the AV nodo has been defined by classical histological methods; however, with recent studies, a more precise characterization of structure is becoming attainable. Dual pathway electrophysiology, one of the hallmarks of the human AV junction, has been widely investigated over the last century [1]. However, the presence of new functionally and anatomically distinct AV pathway was described [2].

The AV node is a part of electrical control system of the heart that coordinates heart rate. It electrically connects atrial and ventricular chambers. The AV node is an area of specialized tissue between the atria and the ventricles of the heart, specifically in the postero-inferior region of the interatrial septum near the opening of the coronary sinus, which conducts the normal electrical impulse from the atria to the ventricles. It is located at the center of Koch's Triangle - a triangle enclosed by the septal leaflet of the tricuspid valve, valve, the coronary sinus, and the membraneous part of the interatrial septum [3]. The AV node receives two inputs from the atria: posteriorly, via the crista terminalis, and anteriorly, via the interatrial septum. AV conduction during normal cardiac rhythm occurs through two different pathways : the first pathway has a slow conduction velocity but shorter refractory period and the second pathway has a faster conduction velocity but longer refractory period [4]. Atrioventricular node reentry is typically induced with anterograde block over the fast pathway and conduction over the slow pathway, with subsequent retrograde conduction over the fast pathway.

II AV Nodal Reentrant Tachycardia

Mendez and Moe (1966) proposed that atrio-nodal connection utilizes alpha and beta pathways that connect together in the distal node [5]. Anatomical and functional studies of the AV node have demonstrated the presence of two distinct input pathways, providing the substrate for clinically important AV nodal reentrant tachy-arrhythmias. In patients with dual AV nodal pathways, a normally timed sinus impulse will conduct through the AV node via beta pathway, since the beta conducts more rapidly than the alpha pathway. However a premature atrial impulse can arrive at the AV node at such a time that the beta pathway is still refractory from the previous normal beat, but the alpha pathway is no longer refractory. This early impulse will then traverse the alpha pathway, reaching the His bundle after a prolonged conduction time through the AV node this AV nodal conduction delay is manifested by a prolonged PR interval on the surface ECG. If the beta pathway recovers by the time the impulse reaches the distal portion of the alpha pathway, the impulse may conduct retrogradely up the beta pathway (producing an atrial echo beat). If this retrograde impulse is then able to reenter the alpha pathway, a continuously circulating impulse can be established within the AV node (Figure 1) [6].

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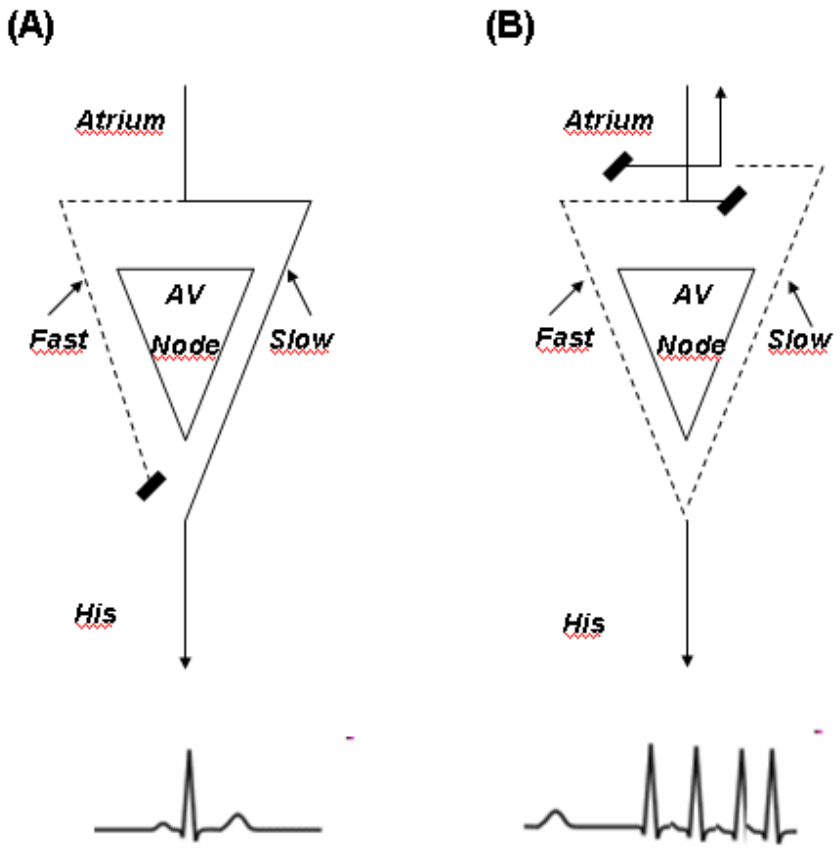

Figure 1. Dual nodal physiology. The atrium, AV node, and His bundle are shown schematically. The AV node is longitudinally dissociated into two pathways, slow and fast, with different functional properties. In each panel of this diagram, solid lines denote excitation in the AV node, which is manifest on the surface electrocardiogram, while dotted lines denote conduction, which is concealed and not apparent on the surface electrocardiogram. (A) During sinus rhythm the impulse from the atrium conducts down both pathways. However, only conduction over the fast pathway is manifest on the surface ECG, producing a normal PR interval. (B) A more premature atrial impulse blocks in the fast pathway, conducting with increased delay in the slow pathway. The impulse conducts retrogradely up the fast pathway producing a single atrial echo. Retrograde conduction occurs over de fast pathway and reentry occurs, producing a sustained tachycardia. The impulse conducts over the slow pathway to the His bundle and ventricles, producing prolonged PR interval on the surface ECG.

Despite the impressive amount of information concerning AV nodal conduction, the role of the AV node in AV block is poorly understood [7]. Electrical stimulation of the vagus nerve in rat induced significant bradycardia, third degree AV block and the P wave appearance was negative in leads II in ECG, suggesting atrial reentry. Morphine injections induce a positive P wave appearance through one inhibitory action on AV nodal reentry [2]. This study sought to describe electrophysiologic characteristic and possible anatomic site of atrial retrograde slow AV node pathways.

III AV Block and Atrial Reentry

Despite the impressive amount of information concerning AV nodal conduction, the role of the AV node in bradycardia is poorly understood. In particular, the spatial and temporal pattern of the AV node engagement from the atria has not been sufficiently studied.

The dromotropic effects of the vagus on atrioventricular conduction are classic and have been studied for a long time. Vagal cardioinhibition is exerted through a reduction not only in the heart rate but also in the rate of propagation of the cardiac action potential and in myocardial contractility. The parasympathetic nervous system innervates the heart through two cervical vagal branches. The right vagal branch mainly influences the heart rate by the modulation of the rhythmogenesis of the sinoatrial node. The left branch predominantly influences the conduction properties of the AV node. Under both types of vagal stimulation protocols, AV blockade appeared most frequently when the left-sided nerves were stimulated first [8].

The unilateral stimulation of the distal segment of left vagus nerve in rats anesthetized with Equitesin®, decreases heart rate and induced significant bradycardia associated with a third degree AV block and negative P wave appearance, consistent with retrograde AV conduction (Figure 2A). The morphine injection induces the appearance of a positive P wave through one inhibitory action on AV nodal reentry (Figure 2B). In the anaesthetized rat, morphine decreased the bradycardia. Presynaptic modulation of neurotransmitter in the regulation of cardiac function was reported by Kosterlitz and Taylor (1959) who demonstrated that morphine reduces the cardiac slowing produced by vagal stimulation [9]. All suggest the presence of a new functionally and anatomically distinct AV pathway [2].

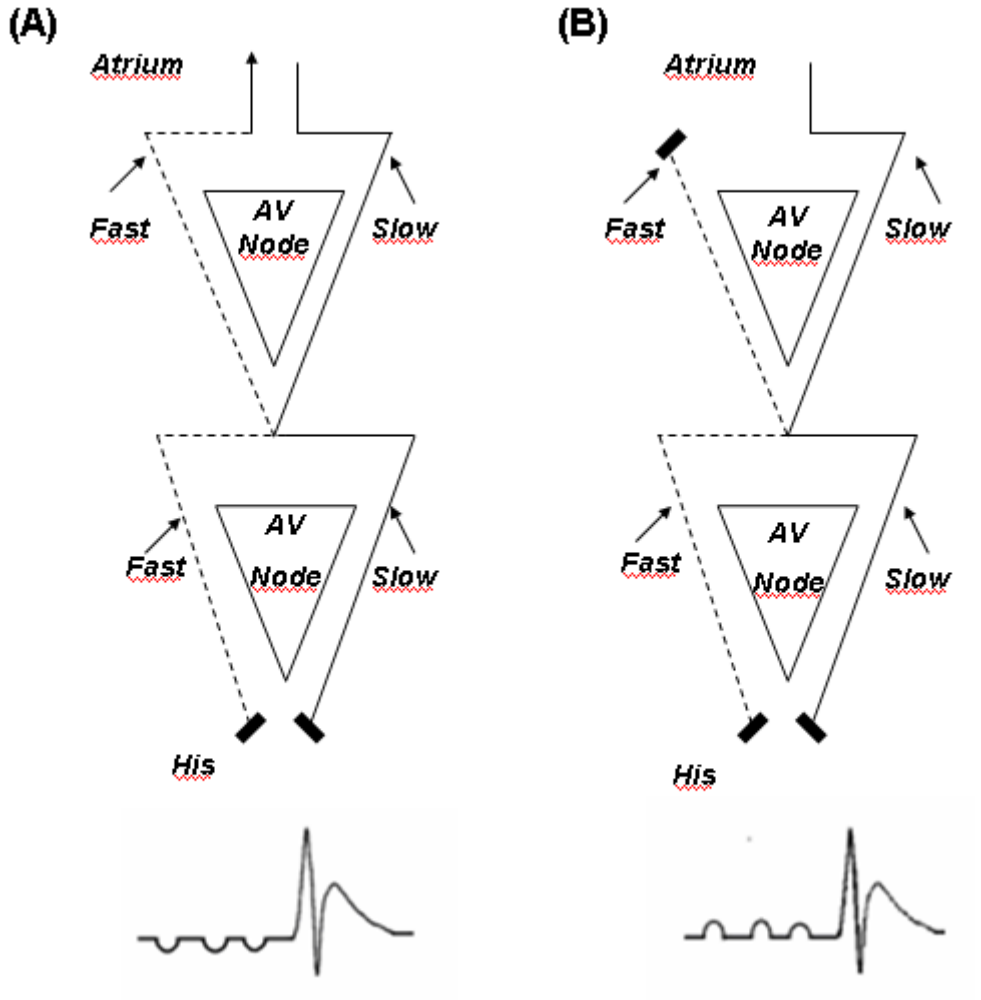

Figure 2. Atrioventricular block and atrial reentry. The figure (A) represents the third degree AV block and negative P wave, suggesting atrial reentry, after electrical stimulation of the vagus. At (B), the P wave wave inversion after treatment of animals with morphine.

The reentry circuits consist of two pathways around the central obstacle: a fast pathway with long refractory period and a slow pathway with short refractory period. During treatment of morphine, the activation signal will travel through both pathways and conflict within the slow pathway. In this case the reentry circuit is equivalent to the fast pathway alone. However, if a premature stimulus enters the circuits before the fast pathway finish its refractory; it will be blocked in the fast pathway and go along the slow pathway, causing significant delay (Figure 2B). If the fast pathway finishes its refractory when the stimulus arrives the circuit exit, the activation wave will go retrogradely along the fast pathway, causing an atrial reentry, during unilateral stimulation of the distal segment of left vagus (Figure 1A).

Spontaneous activity of the mammalian heart is generated in the sino-atrial node. Pacemaker activity is generated in sino-atrial node cells but the regulation by the autonomous nervous system is still a matter of debate. A number of different ion channels and signaling events have been implicated in pacemaker activity [10]. In order to better understand the need and

the operation of the pacemaker, we provide some background. The sino-atrial node potential could also be important for preservation of pacemaker activity in order to generate reentrant atrial. There is a ventricular pacemaker which takes over as the main pacemaker if the AV node fails. After the depolarization of the ventricles, a transient period follows where no further ionic current can be flow through the myocardium. This is known as the refractory period. A recharging (depolarization) of the ventricular myocardium to its resting electrical potential and the heart is then ready to repeat the cycle. The changes in P wave morphology probably result from changes in the sequence of atrial muscle activation arising from a change in the exit site from the SA node. The stimulation of vagus nerve and morphine injection induced a third degree AV block. Third-degree AV block with a ventricular pacemaker is characterized by the complete dissociation of the P waves and the QRS complexes. Under these conditions, there is no PR interval (since the P wave didn't cause the QRS complex). The atria and the ventricles are functioning entirely independently of each other (Figure 2B). The stimulation of vagus nerve induced a significant bradycardia and biphasic the P wave, consistent with retrograde AV conduction (Figure 2A).

Despite the need for a structural and functional correlation in the AV node, the anatomical existence of the substrate for dual pathway electrophysiology is not necessarily indicative of the existence of functional reentry, although required to maintain the reentry circuit. It is apparent that both structural and functional compartmentalization has to exist within the AV node, as revealed by stimulation of vagus nerve and the functional data obtained from ECG. From these data, two distinct pathways or "compartments" are becoming apparent within the AV node, as suggested by stimulation of vagus nerve, that appear to be continuous with the atrial bundle and display distinct conduction properties. With the elucidation of basic elements of both structure and function via investigation, new opportunities are becoming apparent in utilizing the unique properties of AV node for pursuing novel applications relevant to electrophysiology of heart.

IV. Conclusions

Electrical stimulation of the left vagus induced AV block and negative P wave, when morphine was injected the P wave appearance positive through one inhibitory action on AV nodal reentry; suggesting the presence of new functionally and anatomically distinct AV pathway. The proposed system is available as a free and open source platform to the research community.

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Evaluation of Pattern of Magnetic Resonance Images of Lumbo-Sacral Spine in Cameroon - A Pioneer Study

By Dr. Felix U. Uduma, Dr. Pierre Ongolo, Dr. George Assam, Dr. Pius Fokam, Dr. Mathieu Motah

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Abstract - Rationale : Low back pain is a common debilitating disease with negative effect on productivity. Magnetic resonance imaging (MRI) with its excellent soft tissue contrast and absence of bone artefact is the current modality used in evaluating the possible aetiologies of low back pain. MRI availability in Central Africa is recent, with only two existing machines including the newly installed one in Polyclinic Bonanjo, Douala.

Aim : To evaluate lumbo-sacral spine MR images with elucidation of possible causes of low back pain.

Methodology : A pioneer prospective study of patients who were referred to Department of Radiology, Polyclinic Bonanjo, Douala, Cameroon for MRI of the lumbo-sacral spine from June –November, 2009 was done. Equipment used was 0.3Tesla Hitachi AIRIS 11. Sagital, coronal and axial images were acquired. When indicated T1W-Gd-DTPA and STIR were adjunctive sequences used. Patients with either claustrophobia or having MRI incompartible medical implants were excluded.

Results : 48 Patients with age range 20-79 years with mean age of 49.5 were studied. Males were 29(60.4%) and females were 19 (39.6%). The commonest aetiology of low back pain was disc hernia 16(33.3%) with 62,5% occurring at L4/L5 disc level while 25% was at L5/S1. Gender difference decreases with age.

Conclusion : Thus disc herniation is the commonest cause of low back in Cameroon, often accompanied by spondylosis.

Keywords : Lumbo - sacral spine, MRI, Low back pain

GJMR Classification : NLMC Code : WE 725

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I. Introduction

Low back pain is a common referral in routine MRI practice and also a common integral part of the clinical history of patients who present for spinal magnetic resonance imaging (MRI) [1] Imaging serves to bolster the notion that low back pain (LBP) is nothing more than the symptom of an underlying disease.[2]., However, determining the cause of back pain is complicated as it is often multi-factorial and anatomical abnormalities are common in the spine which may not necessarily translate into clinical symptoms [3]. LBP is associated with a wide range of clinical disorders. The commonest group is mechanical disorders, which occurs in more than 90% of all episodes of back pain. [1]. 10% of the remaining patients with back pain have symptoms related to systemic illness like cancer, inflammatory back disease including sacroiliac arthritis or infection [1]

The use of plain radiographs to evaluate patients who have low-back symptoms is indicated when the symptoms have persisted for more than four to eight weeks and are associated with pain at night or at rest[4]. These radiographs are used primarily to rule out infection, malignant lesion, fracture, and inflammatory conditions [4]. Negative results may help to reassure the patient that no major pathological condition exist [4]. But conventional radiography alone cannot conclusively assess the soft tissues of the spine. Thus newer technologies have been quickly adopted with the hope that they will improve our understanding of the physiopathology of the disease and assist us in alleviating patients' pain and discomfort [5]. Such technology is MRI, which is the gold-standard and preferred imaging modality for evaluation of most of the spinal lesions. This is because of its superiority in soft tissue contrast, non-invasiveness, multi-planar imaging capabilities and lack of productions of ionizing radiations] [3,6,7]. The high resolution of MRI for soft tissues allows elucidation of the morphology of the inter-vertebral disc, the nerve roots, the contents of the central spinal canal, foraminae and the facet joints [3]. Coronal and sagital acquisitions can easily be made unlike computed tomography (CT) that needs reconstruction to reproduce similar images. CT imaging may be unwarranted and may also be objectionable for younger women, since it may unnecessarily exposes patients to ionizing radiation[8] The current guideline designate MRI as the first choice of investigation of herniated nucleosi pulposi and suggested CT as the alternative in the evaluation of lumbar back pain if MRI is contraindicated or unavailable[9]. Besides herniated disc, the direct evaluation of nerve roots by MRI has been considered an important asset to facilitate decision making in patients with back pain [9]. The presentation of lesions in LBP involving various lumbar

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spinal structures as well as sacroiliac joint often overlap and are clinically indistinguishable, necessitating evaluation by MRI[1]. Magnetic resonance imaging (MRI) is increasingly requested for people with LBP and has diverse utility in evaluating spinal lesions connected to LBP [3]. It has an acknowledged role in diagnosing serious spinal pathology, planning surgical management in cases of radiculopathy and spinal stenosis [3]. MRI has been tested as a screening tool to assess the risk of people in different occupations developing LBP [3] MRI plays a useful role in patients with early disease, by its superior ability to directly image changes in articular cartilage [1]. It has revealed lumbar disc abnormalities in up to three-quarters of asymptomatic subjects, including those with no previous history of LBP, sciatica or neurogenic claudication [3] MRI of the spine is useful for detecting occult compression of the spinal cord or cauda equina in patients with skeletal metastases and back pain, allowing treatment to be instituted before the onset of neurological complications. [3]. It is also the technique of choice on evaluation of bone metastasis as it is sensitive to early marrow changes that precedes osteoblastic response in the bone matrix of some malignancies [10].

However, low specificity limits the diagnostic utility of MRI scans[2] It cannot be used to predict back pain which are insensitive to anatomical changes that might correlate with new symptoms[2] Imaging can also lead to the identification of pathology unrelated to a patient's LBP[or find patho-anatomical abnormalities that have little or no correlation with patient symptoms[8]. The current role of MRI in back pain is encapsulated in the RCR (Royal College of Radiologists) guidelines and the joint clinical practice guidelines from the American College of Physicians and the American Pain Society.[3] The guidelines discourage routine imaging in patients with non-specific LBP and counsel reserving its use for cases in which severe or progressive neurological deficits are present or serious underlying conditions are suspected[3].

II. Aims

To analyse the MRI findings of the lumbo-sacral spine so as to evaluate the commonest pathologies in low back pain in Cameroon.

III. Materials and Method

a) Patients

Forty-eight patients with an age range 20-79 years with low back pain underwent MR imaging during a period from June, 2009 to November, 2009. All patients were evaluated in detail by clinical and spine examination prior to MRI lumbo-sacral region. The eligibility criteria included (a) the chief complaint of LBP- encompassing idiopathic, mechanical, inflammatory, infective, post operative causes, others and not merely to mechanical or inflammatory group. This was done intentionally to include a large cohort referred for MRI lumbar spine. (b) there was no contraindications to MR imaging (e.g. pacemaker, aneurysmal clips, foreign body in globe etc).

b) MRI Protocol

MR imaging was performed at our hospital, using 0.3 Tesla Hitachi AIRIS 11 MRI machine, and spine phased-array coil. Technical factors used were T1W, T2W, STIR. Sagital acquisitions were used in screening while axial and coronal were used to evaluate the neural foramina. This was followed by T2 STIR images acquired in oblique coronal and sagital planes .Enhanced T1W images with Gadolinium pentate dimeglumine were used in cases of intra-spinal mass lesion or to evaluate herniated disc lesions where T2W images were degraded.

Technical specifications included a slice thickness of 3 and 4 mm for sagittal and axial sequences, respectively; a field of view of 26 and 20 cm for the sagittal and axial images, respectively; and a matrix of 192 by 256. The T_1- and T_2 weighted axial sequences were stacked slices extending from the inferior aspect of L3 through the inferior aspect of S1.

c) Data Collection and Results

Forty-eight patients with an age range 20-79years with mean age of 49.5 years with low back ache underwent MR imaging during a period from June, 2009 to Novenber, 2009. Quantitative results were analysed using SSPS PC.

Males were 29(60.4%) and females 19(39.6%). Males to female ratio of the studied population was 1.5:1. The patients referred were not from a single clinical specialist source, but from multiple specialties like orthopaedics, paediatrics, rheumatology, neurology, neurosurgery and general medicine. The highest number of studied cases belonged to 50-59 year age range with 31.25%, and male to female ratio of 1:1.14. The second highest studied range is 40-49years (29%) with male to female ratio of 1:0.4. The commonest pathology is disc hernia, 16 cases (33.3%) with male to female ratio of 3:1. Spondylosis without any evidence of disc hernia was high with 12 cases (25%). 62.5% of herniated disc occurred at L4/L5 disc level followed by 25% at L5/S1 disc level. At L4/L5 level male to female ratio is 4:1 while it is 1:1 at L5/S1

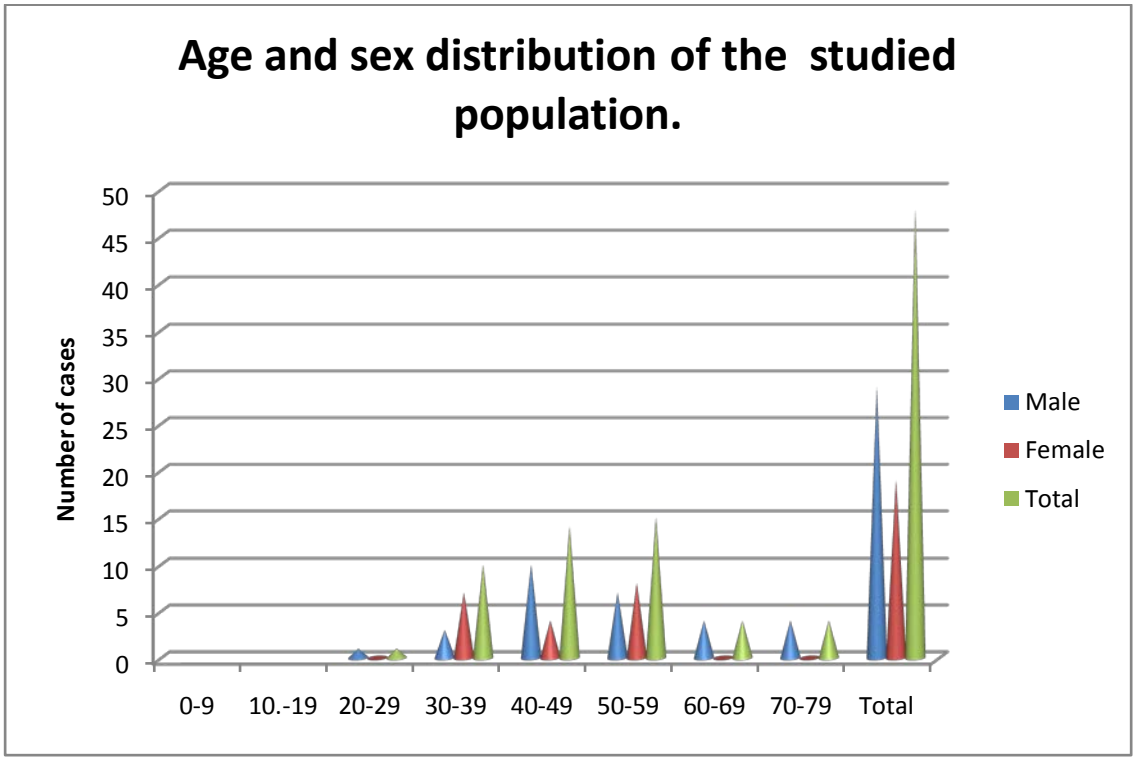

Fig. 1

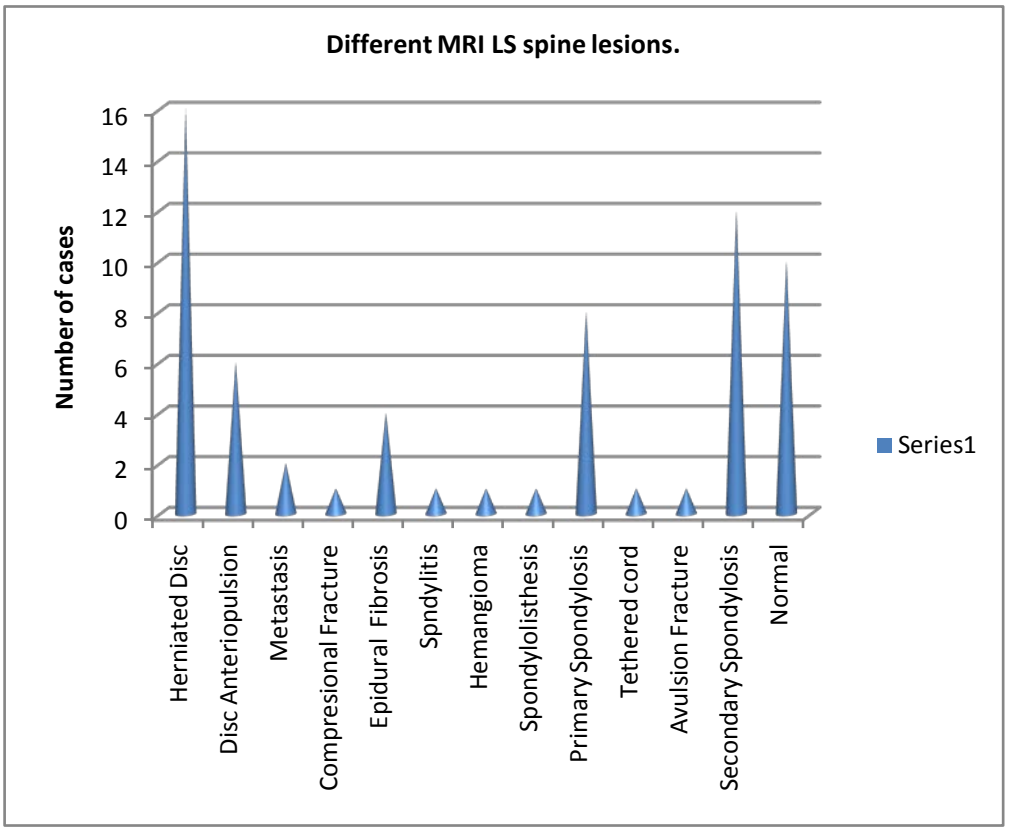

Fig. 2

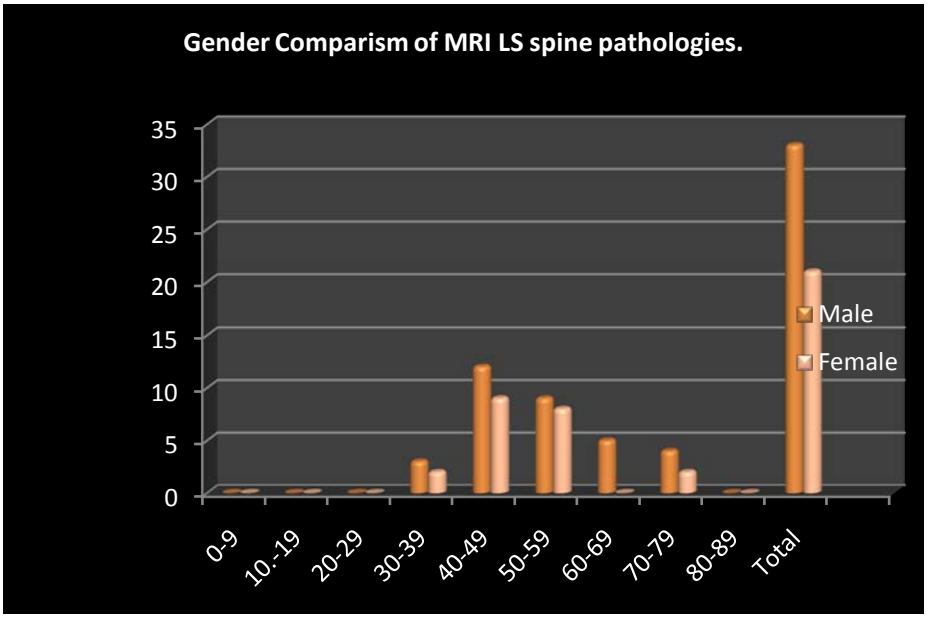

Fig. 3

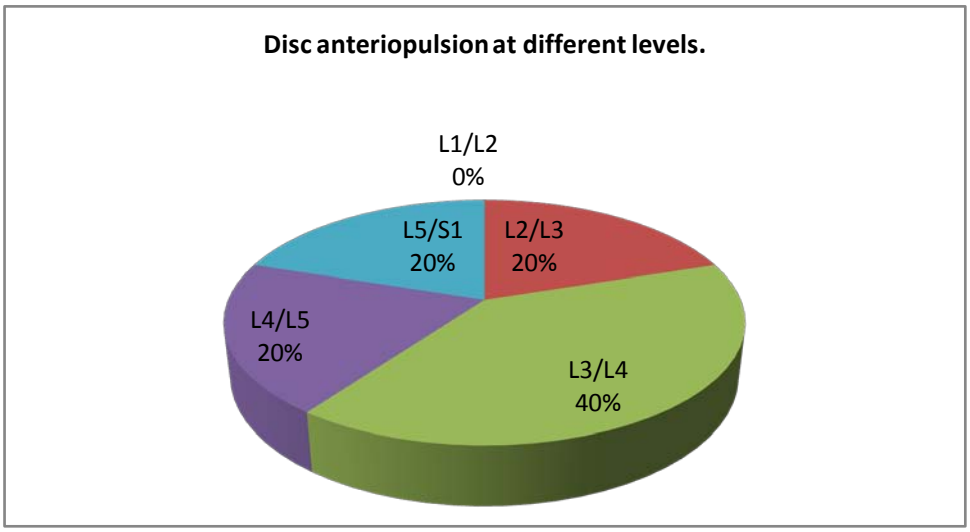

Fig. 4

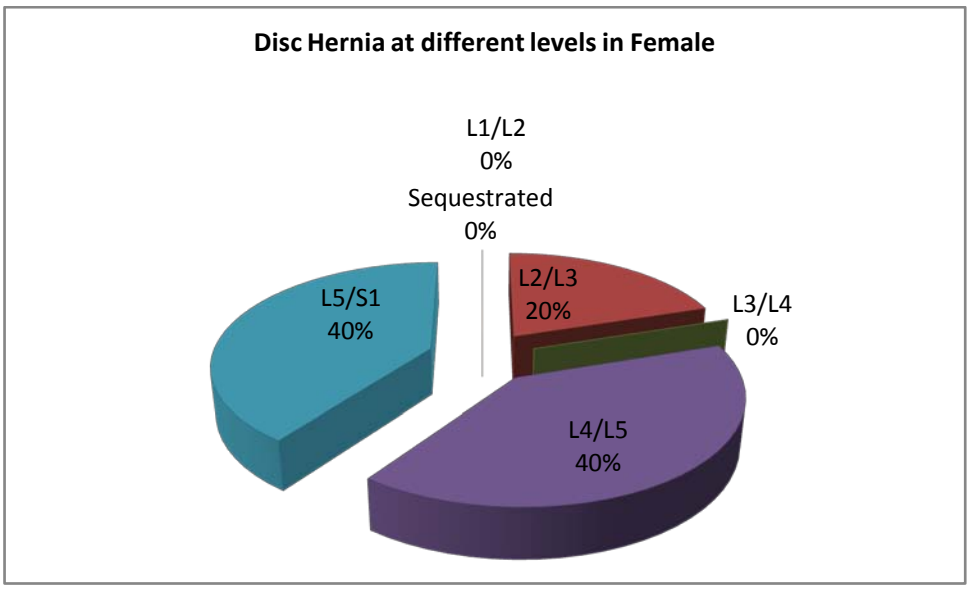

Fig. 5

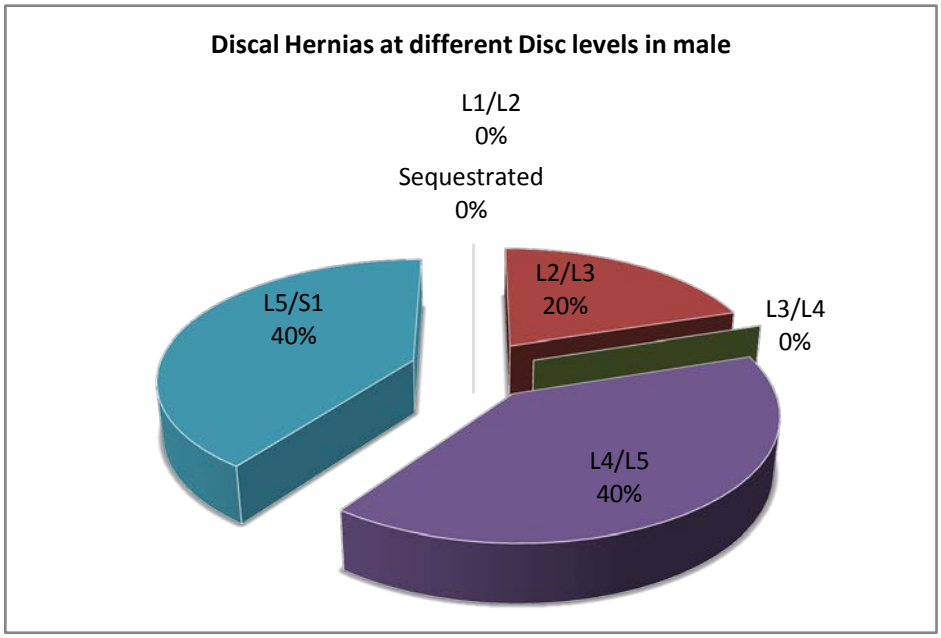

Fig. 6

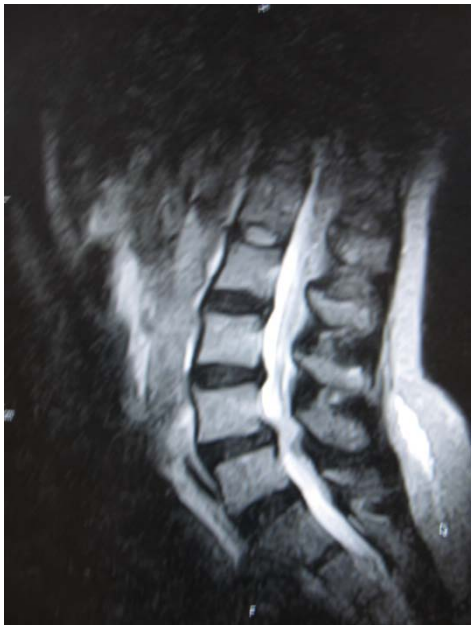

Fig. 7 : Mid - sagital T1W MRI showing L3/L4 disc hernia.

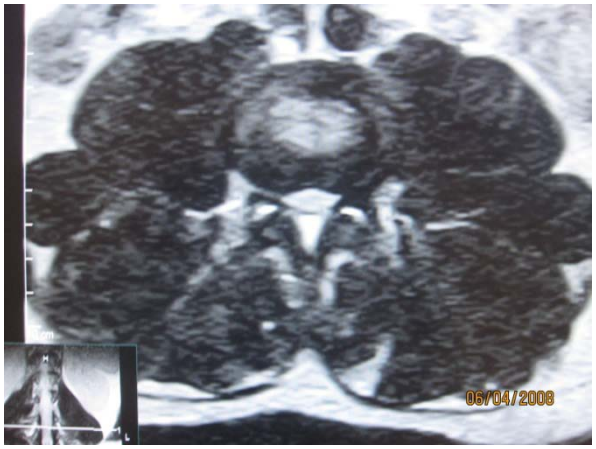

Fig. 8 : Axial T1W showing Lumbar stenosis and left nerve root compression

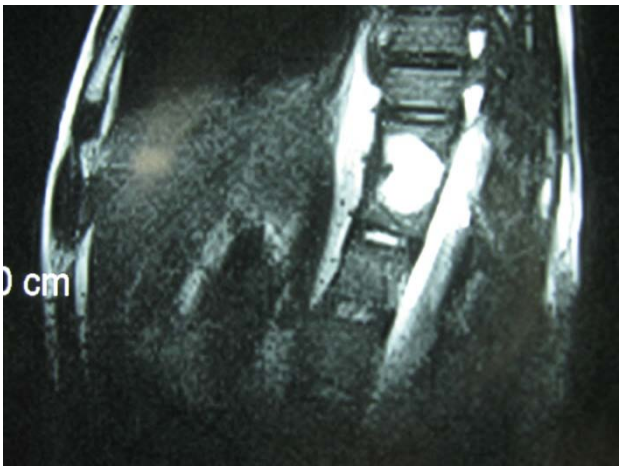

Fig. 9 : Midsagital T2W MRI showing hyperintense lesion

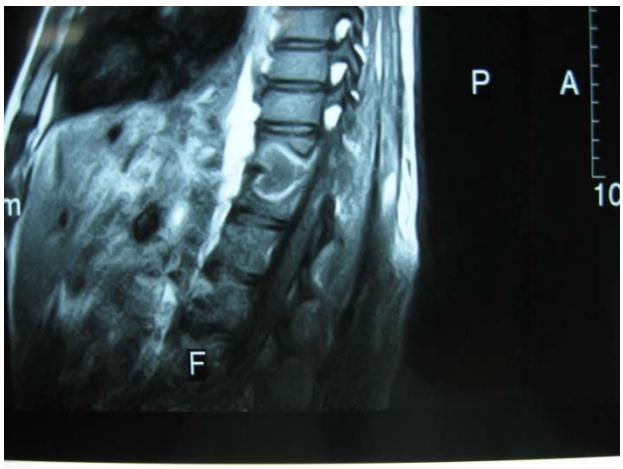

Fig. 10 : Mid-sagital Enhanced T1W MRI showing ring enhancement of the above Spondylo-discitis affecting two contiguous vertebrae of Spondylo-discitis

IV. Discussion

Low backache is a common clinical presentation in medical practice and MRI centres [1]. It has been observed that in any 12-month period in USA, 15% to 20% of the population has an episode of lumbo-sacral pain.[1,4]. In a larger context, the prevalence of back pain over the course of lifetime in the entire population of industrialised societies is more than 70 percent.[4,11]. For example, the lifetime prevalence of LBP is approximately 80 percent in Americans [11]. LBP is second only to the common cold as the reason patients cite for seeking medical care [11].

This pioneer prospective MRI study is paramount because of paucity of such documentations in central African region. Our centre is the second MRI centre in Central African region and the earlier machine in another centre had broken down without any documentations of MRI findings related to LBP. MRI defines the lumbo-sacral spine diagnosis with high specificity allowing the most approximate therapeutic decisions [9].

Back pain is the most frequent cause of limitation of activity among individuals who are lessthan forty-five years old.[4]. Our largest studied population with low back pain, 31.25% was in the 50-59 age range with male to female ratio of 1:1.14. This is followed by 29% in the 40-49 age range with male to female ratio of 1:0.4. This agreed with high incidence of low back pain in the work force with attendant negative impact on productivity and economy [1].Annually, back symptoms occur in 50% of working age adults in USA [1]. Each year, there are approximately 500,000 Workers' Compensation and personal-injury cases dealing with low-back pain [4]. In this study, detected number of pathologies outweigh the number of studied population. This is because multiple pathologies can exist in one patient.

a) Disc Lesions :

The high signal intensity of the cerebrospinal fluid and epidural fat in T2W sequence makes T2W sequence the most useful in evaluation of discal lesion, which is dorminant pathology as in our study [9]. The commonest pathology in this study is disc hernia with 16 cases (33.3%) with male to female ratio of 3:1. 10 cases (62.5%) of herniated disc occurred at L4/L5 disc level followed by 4 cases (25%) at L5/S1 disc level. At L4/L5 level male to female ratio is 4:1 while equal male to female ratio is seen at L5/S1 level. This predominance of disc herniation at L4/L5 and L5/S1 levels is supported by previous study [12] The reducing gender difference is accounted for by the increasing degeneration, laxity, demineralisation and dessication with ageing in both sexes [9]. This is corroborated by the articular facet degenerative changes seen in almost all cases of disc herniations shown as height reduction and subluxation of the ligamentum flavum of the facet joints[9,12].

Disc herniation can be used to describe a wide spectrum of abnormalities involving disk extension beyond the interspace, from a bulge to a frank extrusion and sequestration; [11]. The terms used to classify disks were defined as follows: normal, no disk extension beyond the interspace; bulge, circumferential symmetric extension of the disk beyond the interspace (around the end plates); protrusion, focal or asymmetric extension of the disk beyond the interspace, with the base against the disk of origin broader than any other dimension of the protrusion; and extrusion, more extreme extension of the disk beyond the interspace, with the base against the disk of origin narrower than the diameter of the extruding material itself or with no connection between the material and the disk of origin[9,11].Sequestered disc are free disc fragment which may migrate below or above the interspace [6]. On MRI examination of the lumbar spine, many people without LBP have disk bulges or protrusions but not extrusions, thus discovery by MRI of bulges or protrusions in people with LBP may frequently be coincidental [11]. There is a hypothesis that the prevalence of extrusions in people with symptoms of LBP may be substantially higher than in people without symptoms [11]. Sequestered or free fragment has high $T2^{*}W$ signal because their increased water content produces an increase in signal intensity [6]. When it is behind the parent disc, it is round in configuration but oblong on further separation [6]. Annular defects or fissure which can be demonstrated by MRI as decreased signal on the T_2-weighted image may be a fore-runner to disc hernia and are frequently asymptomatic[11] But any pain , possibly results from leakage of the contents of the nucleus pulposus into the epidural space, with related nerve irritation[11]. The reported prevalence of posterior radial tears at autopsy in asymptomatic people is 40 percent for those between the ages of 50 and 60 years and 75 percent for those between 60 and 70 [11].

In our study, no distinction was made between disc protusion and extrusion, rather cases where there is protusion of disc anteriorly and behind anterior longitudinal ligament was considered separately and termed disc anteropulsion. 6 cases (12.5%) anteropulsions were seen. Using MRI in 67 people without symptoms, Boden et al. found herniated disks in 20 percent of the people less than 60 years old and in 36 percent of those 60 years of age or older [11]. But our study included symptomatology criterion and discovered 60% of patients 60years and above had disc hernia. Low back ache is one of the most common causes of morbidity in elderly patients and could be due to multiple aetiologies like degenerative-inflammatory lumbar spinal pathology .[2,13] Multiple levels of disc hernia was seen in 56.25% of our patients. MRI examination of 41 women without symptoms showed that 54 percent had a disk bulge or herniation at one or more disk spaces, although only L3-4, L4-5, and L5-1 levels were examined [11].

b) Lumbar Stenosis :

MRI is the preferred investigation for confirming lumbar disc herniation, nerve root entrapment, radiculopathy, and spinal canal stenosis [3]. Lumbar spine stenosis (LSS) is subdivided into relative and absolute LSS according to the anterior–posterior diameter of the spinal canal (physiological value is 22–25 mm) [7]. Relative LSS is when spinal canal measures 10–12 mm in diameter and usually asymptomatic. Whereas absolute LSS (spinal canal <10 mm in diameter) is often symptomatic and is associated with absence of free subarachnoid space [7]. The lateral recess can also be considered in LSS definition (physiological diameter is 3–5 mm) and stenosis is considered if it has a diameter of <2 mm [7]. 32(66.66%) of our studied population had lumbar stenosis. LSS can be mono-segmental or multi-segmental, and unilateral or bilateral. Patho-anatomically, stenosis can be classified as central, lateral or foraminal. This is often the sequllae of degenerative disc hernia [7]. Herniated disc is classified into central, centro-lateral and lateral, the commonest is centro-lateral. [6]. Laterally herniated discs and smaller focal disc herniations may be difficult to diagnose with only sagital imaging. Axial imaging will help and has become a routine examination protocol to assess the degree of lateral, neural canal, nerve root and cord involvement [12]. Depending on the extent of the degeneration, central, lateral and foraminal stenosis can occur alone or in combination. The L4–5 spinal discs are most frequently affected by LSS, followed by L3–4, L5–S1, and L1–2[7].This highest occurrence of lumbar stenosis at L4/L5 is noted in our study with disc hernia being the predominant culprit. The frequency of degenerative LSS diagnosis has risen over time, as a result of increasing lifespan and demand for a better

quality of life, awareness of the disease, and the availability of advanced imaging techniques. [7].

Multiple factors can contribute to the patho - genesis of spinal stenosis, and these can act synergistically to exacerbate the LSS [7].Central stenosis results from degeneration and protusion of the disc, which leads to ventral narrowing of the spinal canal [7]. Foraminal stenosis is a consequence of disc degeneration, with further reduction of the height of the intervertebral space, leading to narrowing of the recess and intervertebral foramina, exerting strain on the facet joints [7]. Such an increase in load leads to facet joint arthrosis, hypertrophy of the joint capsules and the development of expanding joint cysts (lateral stenosis), which in combination propagate spinal instability [7]. Central stenosis is further contributed by the reduced height of the segment and the ligamenta flava forming creases, which exert pressure on the spinal dura from the dorsal side [7]. Concomitant instability due to loosened tendons (for example, the ligamenta flava) further propagates pre-existing hypertrophic changes in the soft tissue and osteophytes, creating the characteristic trefoil-shaped narrowing of the central canal. [7]

The clinical features of the condition are heterogeneous, and often, include neurogenic claudication which comprises limping or cramping lumbar pain that radiates into the legs primarily during walking [7]. Degenerative LSS can ultimately lead to the compression of individual nerve roots, the meninges, the intraspinal vessels, and, in exceptional cases, the cauda equine [7] Nerve root compression triggers localized inflammation, which affects the nerve root's excitatory state. [7] In addition, two interdependent vascular mechanisms are hypothesized to assist in the development of neurogenic claudication in LSS: reduced arterial blood flow resulting in ischemia, and venous congestion with compression of the nerves and secondary perfusion deficiency [7]. — Conversely, compressive radiculopathy can cause autonomic dysregulation and impaired circulation in the legs [7]. The extent of compression is increased by hyperextension or hyperlordosis of the lumbar spine, because these postures cause additional narrowing of the spinal canal. [7]. Where as hyperflexion abrogates lordosis, resulting in a widening of the spinal canal [7]. The development of cauda equina syndrome, which comprises sacral hypesthesia, loss of tendon reflexes in the lower limbs and incontinence, as a result of LSS is only found in exceptional cases [7] In cases of lateral recess stenosis or foraminal stenosis, isolated radiculopathy can occur [7].

c) Epidural Fibrosis :

Epidural fibrosis and recurrent or persistent disc herniations are the two most common causes of failed back syndrome, seen in 10-40% of post surgical patients[6[Pre- and post-enhancement T1W images are very sensitive in this differentiations since fibrosis enhances and recurrent disc does not[6]. 6.25% of our studied population had epidural fibrosis.

d) Spondylosis :

It is well known that magnetic resonance imaging is the most sensitive imaging method for the evaluation of spinal degenerative pathology, even in the initial stages of the disease [14]. Many authors have believed that a degenerated disc is the most likely source of chronic, disabling LBP (discogenic pain, internal disc disruption [4]

Degeneration of the lumbar spine occurs in three phases : dysfunction (progressivetearing of the annulus fibrosus, degeneration of the nucleus pulposus, and arthropathy of the facet joints), instability (laxity of the facet joints, ligaments, and discs), and restabilization (formation of osteophytes and hypertrophy of the facet joints [4].18(37.5%) of our studied population had spondylosis. Spondylosis was subdivided in our study into primary or secondary with a ratio of 1:1.57. Secondary spondylosis is predated by a pre-existing aetiologies like mechanical impact on a vertebra, spondylolysis and spondylolisthesis. [6,12] This is commonest in the lumbo-sacral spine[12]. MRI features of spondylosis are disc cartilage loss in height with T2W hypointesity of dessication, T1W linear signal void of vacuum phenomenon in the disc cartilages, osteophytosis, end-plate sclerosis, marrow changes sometimes schmorl's nodules.[6,7]. MRI accurately delineates the cardinal features of spondylosis, like changes in joint space width and symmetry, presence of erosions, subchondral edema, spondylophytes, sclerosis, cysts and ankylosis [1]. MRI sensitivity of end-plate changes for discogenic pain is low[3] Furthermore, Comparative studies between MRI and CT in the evaluation of sensitivity and specificity of MR for the detection of cortical erosions and subchondral sclerosis when compared to CT images were 100 and 94.3%, respectively[1]. .

e) Spondylolisthesis

Whenever a spinal disc vertebrae slips to the front or the back of the spine in comparison to the other vertebrae it is termed "spondylolisthesis"[15]. It is commonest at L4 on L5[16] When the *vertebrae goes forward in the spine it is known as "anterolisthesis" and whenever the vertebrae goes backward in the spine it is known as "retrolisthesis* [15,16]*. Both anterolisthesis and retrolisthesis are spinal defects that can cause the patient pain in the back.* [15] There are five types of the condition. These are dyspastic spondylolisthesis, pathologic spondylolisthesis, traumatic spondylolisthesis, degenerative spondylolisthesis, and isthmic spondylolisthesis [15] _ Type 1 - (dyspastic spondylolisthesis) is congenital and due to dysplasia of

the neural arch wlth adolescent symptomatology. Type 1 is when there is a defect in the facet formation of a vertebra that lets it slip to the front [15] Type 2 is isthmic spondylolisthesis due to defect in pars inter-articularis following stress fracture [16,]. Type 3 is Degenerative spondylolisthesis and due to degeneration of pars inter-articularis [15]. When there are tumors or other abnormalities in the bone itself of the vertebra then it is called pathologic spondylolisthesis. [15].

When there is trauma to a specific vertebra or any type of vertebra injury sustained then it is termed traumatic spondylolisthesis. The injuries are typically to the facet joints or to the pedicle of the bone formation. [15]. All these manifest in five grades of advancement of spondylolisthesis,: Grade 1 - 25% of the body of the vertebra has slipped, Grade 2 - 50% of the body of the vertebra has slipped; Grade 3 - 75% of the body of the vertebra has slipped, Grade 4 - 100% of the body of the vertebra has slipped; Grade 5 - The body of the vertebra has fallen off completely [15,16]. Presenting symptoms and signs are back pain, nerve root compression and spinal stenosis. Spondylolisthesis is corroborated by visualization in MRI of spondylolysis. But it may be difficult because MRI is insensitive to sclerosis which usually outlines or corticate the lysis in pars inter-articularis [16].This difficulty is averted by conventional radiography or computed tomographic studie [16].

f) Vertebral Trauma

Vertebral trauma may present as avulsion or compressional fractures. 2.08% of our studied population had compression fracture and another 2.08% had avulsion fracture. Compression could be spontaneous, traumatic or osteoporotic. Osteoporosis increases steadily with age, ranging from 20% for 50year old women to 65% for older women [17]. 50% of spinal traumas occur in the thorax, lumbar and sacral and the other 50% in cervical vertebra [17] For the stability of spinal fractures, there are three functional columns of the spine. Anterior column is made up of anterior half of both the vertebral body, disc and anterior longitudinal ligament [6]. Middle column is the posterior half of vertebral body/disc and posterior longitudinal ligament. Posterior column contains the neural arch and ligaments. Disruptions of two or more ligaments results in unstable fracture [17].

g) Spondylo-Discitis

Spondylo-discitis is seen in 2/100,000 per year, most common in patients older than 65years, diabetes mellitus or immunocompromised[18]. Such rarity is evidenced in this study with detection of only a case (2.08%). This aptly demonstrated the characteristic ring enhancement and involvement of two adjacent vertebrae. Spondylo-discitis presents as T1W low signal intensity in at least two adjacent vertebrae with sub-ligamentous or epidural soft tissue masses, bony cortical erosion and narrowed disc [18]

h) Vertebral Neoplasm

The metastatic bony lesion seen in our study which occurred in the 6th and 7th decades of life agreed with other studies [10]. Primary origin of vertebral metastasis are lungs (31%), breast (24%), GIT(9%), Prostate (8%) , lymphoma (6%), melanoma (4%) unknown(2%), kidney (1%), others including multiple myeloma (13%). Primary routes are nutrient artery, retrograde spread through Batson plexus (Valsalva manoeuvre) and inter-vertebral foramina [10]. About 70% of symptomatic metastasis found are contiguous segment involvement[10]. Vertebral metastasis seen in this study was from prostrate. Metastasis from cancer of prostrate affects the red marrow bones with 90% skeletal like spine, pelvis, ribs and skull. [10] Messiou et al in their study of osseous metastasis from prostrate, found 70.9% osteoblastic and 29.1% as either lytic or mixed. This skeletal metastasis are diagnosed with conventional radiography or ^{99m}Tc-MDP scintigraphy. Imaging of metastasis to the bones from cancer of the prostrate involves a cascade of studies, starting with ^{99m}Tc-MDP, backed up by plain x-ray correlation and followed by MRI, CT or even PET/CT. Sctingraphy can detect 10% change in bone mineral turnover whereas 50% change is needed for x-ray detection[10]. Sctingraphy can reveal bone metastasis 18months before plain x-ray. But sctingraphy is often not suitable for assessment of therapeutic response due to Flare phenomenon resulting from under-estimation [10]. This is substituted by PSA (prostatic surface antigen) and MRI. This is detected as low T1W signal contrasting with the high signal of marrow fat. The conspicuity is better shown with STIR sequence [10]. Most of the lesions are localised at anterior portion of the vertebral body (60%) while 30% infilterate the pedicle or lamina with small percentage affecting both intra-dural or intra-medullary involvement suggesting poor prognosis. The outcome of metastasis of cancer of prostrate to the spine and associated structures are uniformly bleak with median survival duration of 10months [10]

i) Miscellaneous Causes

Facet arthropathy, sciatica, sacro-iliatis, Baastrup's disease, compression of the nerve roots/spinal cord by osseous spurs or soft tissue structures, posterior vertebral compartment syndrome and intra-spinal lipoma are often overlooked source of LBP [1,2,3,11,13,19,20,21],. Myelo - CT and MRI are extremely useful in myelographic stop (the upper extension of the cord lesion) definition [19]. Fat suppression causes rescaling of signal intensities and categorises cartilage as the brightest structure [1]. This additive effect along with the darkened appearance of fat in adjacent soft tissues, sacral, iliac and lumbar marrow, renders improved visualization of structures and increases the conspicuity of lesion, thereby

improving pickup rate of sacroilitis.[1] There are two fat suppressed sequences that are available: T1-weighted with fat suppression (T1FS) and fast short tau inversion recovery (Fast STIR) sequences. These are superior to T1 and T2 images, in demonstrating the changes of sacroiliitis[1]. MRI of the lumbar spine can clearly depict Baastrup's disease, interspinous bursal fluid, and an associated posterocentral epidural cyst. [13]. In 1929, Brailsford described arthritic joints between the spinous processes on radiological assessment and noted that "such patients have pain in the back when standing erect which is relieved by bending forward [13]. In 1933, Christian Baastrup, a Danish radiologist described in detail the clinical and radiological features of the syndrome. It manifests clinically as localized midline lumbar tenderness and pain on spinal extension that can be relieved by spinal flexion, local anaesthetic injection and excision of part of the involved spinous processes [13]. Radiologically, the disorder is characterized by close approximation and contact of the adjacent spinous processes (kissing spines) and resultant enlargement, flattening and reactive sclerosis of apposing interspinous surfaces [13]. Hypertrophy of the tips of the spinous processes may occur in the elderly persons especially in those with an occupational history of long periods of back flexion. This condition heretofore arises from chronic postural hyperlordosis and regional loss of discal spacings. [13].

Synonyms of Baarstrup's disease are Baastrup's syndrome, Machete's syndrome, Arthrosis interspinosa, diarthrosis interspinosa, kissing osteophytes, kissing spine, kissing spinous disease, osteoarthrosis processus spinosi vertebrarum lumbalum, osteoarthrosis interspinalis [13].

Posterior vertebral compartment syndrome is a non-radicular low back pain, arising from changes of the posterior elements/perispinal tissues of the lumbar spine (i.e., the "posterior vertebral compartment"). They include: facet joint pathology (e.g., osteoarthritis, joint effusion, synovitis and synovial cysts), spondylolysis, spinal/perispinal ligamentous degenerative-inflammatory changes and perispinal muscular changes [2]. T2-weighted sequences with fat saturation, and when indicated the use of contrast-enhanced T1-weighted images with fat saturation, permit the visualization of degenerative-inflammatory changes of the posterior elements of the lumbar spine that in most cases would have been overlooked with conventional non-fat suppressed imaging.[15]

Sacroiliac joint lesions accounts for a small but significant number of LBP [1]. Easy detectability of sacroilitis highlights the diagnostic value and utility of adding a single 'fat suppressed' sequence of the lumbo-sacral region in the coronal plane [1]. This adds marginally to the scan time but increases the yield of identifying incidental or manifest sacroiliac involvement in all cases referred for MRI for LBP [1].

Treatment of LBP could be pharmacological or non-pharmacological. Non-pharmacological interventions include, intensive interdisciplinary rehabilitation interventions—therapeutic exercise, soft-tissue manual techniques, acupuncture, movement re-education techniques, spinal manipulation, cognitive-behavioural therapy, or progressive relaxation.[8]. Morphological abnormality detected on MRI can be augmented with provocative discography to elicit pain response and this will assist in prediction of patients who will benefit from operative stabilization through precise lesion site localization. [4]

LBP is one of the most common causes of physician visits in the United States with an enormous socioeconomic burden [5] The estimated cost of medical care for patients with LBP exceeds $8 billion annually [11]. Over the past 30 years the rate of disability claims related to low back pain has increased by 14 times the rate of population growth[1].[11]

V. Conclusion

The commonest cause of low back pain is disc hernia. Disc hernia in turn is most prevalent at L4/L5 disc level. Multiple pathologies were seen in some patients with common accompaniment being spondylosis and lumbar stenosis.

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Uncommon Types of Disc Hernia (A Report of Three Cases and Review of Literature)

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Abstract - Background : Spinal disc hernia is prolapse of nucleus pulposus through a defect in annulus fibrosus. Over 90% of cases occur in the lumbar spine with only 1% being thoracic. Sequestered disc hernia is the last spectrum of progression of disc hernia with formation of mobile free fragment.

Aim : To add to literature documentation of uncommon types of disc hernia

Case Reports : *CASE 1 :* A 63year old Cameroonian man with L4/L5 sequestered disc hernia, seen posterior to L5 vertebral body. He had discectomy and symptomatic reliefs were better than pre-operative status conforming to McCulloch's clinical outcome grade 3.

CASE 2 : A 34year old male Cameroonian with chronic back pain and paraesthesia following trauma. Thoracic spine Magnetic resonance imaging (MRI) revealed T11/T12 disc hernia with severe epidural compression. He declined discectomy for an Overseas treatment.

CASE 3 : A 72year old male Nigerian who had L3/L4 iatrogenic spinal fusion 5years ago. Lumbo-sacral spine MRI following recurrent low back pain showed L2/L3 and L4/L5 disc hernias. The L2/L3 hernia above the bony ankylosis interestingly is severer than L4/L5 hernia. He was managed conservatively.

Conclusion : MRI increasing availability in Central Africa will detect more cases of uncommon types of disc hernias.

Keywords : Disc, Hernia, MRI.

GJMR Classification : NLMC Code : WI 950

Strictly as per the compliance and regulations of:

Uncommon Types of Disc Hernia (A Report of Three Cases and Review of Literature)

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I. Introduction

Magnetic resonance imaging (MRI) is a non-invasive, multi - planar, neuro - diagnostic imaging tool with superiority in excellent soft tissue contrast [1]. Exoneration from bony artifacts is an added advantage in MRI anatomical evaluation of the spine. MRI has become very useful in anatomical evaluation of thoracic disc hernias as its symptoms are non-characteristic [2].

Disc cartilages are the supportive fibrous cartilage of the entire spine. Disc hernia is a degenerative process in which the gel-like centre of disc cartilage called nucleus pulposus ruptures through the tougher outer wall of the annulus fibrosus.[3]. The tougher peripheral annulus fibrosus protects the inner nucleus pulposus from evisceration. But with increasing age and onset of cartilage degeneration and desiccations, disc herniation ensues. Aetiologies are mainly degenerative or traumatic [3].

The commonest site of disc herniations is in the lumbar spine[1,4]. The site of predilection is L4/L5 disc cartilage[3]. While over 90% of all disc herniation occur in the lumbar spine, the cervical and thoracic spine disc herniations are uncommon.[4,5,6]. The incidence of thoracic disc herniation is reported to be one per million per year [2]

The symptomatology is usually pain and neurological deficits related to the anatomical localization of the disc herniation. Lumbar disc hernia is the commonest cause of low back pain[7].

AIM : To add to available literature documentations of three types of uncommon disc hernias.

SETTINGS: Polyclinic Bonanjo, Douala.

II. Case Reports

a) Case Report 1

F K is a 63 year old male Cameroonian with 2 year history of chronic low back pain that has become un-responsive to usual intake of non-steroidal anti-inflammatory drugs (NSAID). He has normal bladder and bowel control , but has L5 dermatone sensory loss and grade 4 right lower limb power. Straight leg raising test (Lasegue's test) was restricted to 60 ^{0} on the right and 90^o on the left leg. Lumbo-sacral MRI showed 10.9 X8.7mm ovoid material that is isointense to the parent disc and posterior-lateral to the right of L5 vertebral body (FIG 1&2) with type 2 end - plate changes. Axial images (FIG 2) showed compromise of right neural foramen at L4/L5 . Spondylotic changes were confirmed by lumbo - sacral radiograph. A diagnosis of L4/L5 sequestrated disc hernia into L5 spinal canal with secondary spondylosis was made. He underwent disectomy and patient had a relief of discomfort better than pre-operative status (McCulloch's clinical outcome grade 3). He failed to come for 6 months post-operative MRI.

b) Case Reports 2

M L is a 34 year old male Cameroonian with chronic low back pain for 2 years due to a hit on the back by a trainee in Karate sport. This led to lower limb weakness and crutches-assisted mobility . Sensory loss from T10 dermatone with hyperactive Achilles' tendon

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and patellar reflexes were noted. Upper limb showed reduced power but normal sensations. MRI of the thoracic spine showed significant T11/T12 disc hernia (FIG 3). Cervical MRI showed spondylotic changes with posterior osteophytosis on C4-T1. Bilateral narrowing of C5/C6 and C6/C7 neural foramina were shown in the MRI axial acquisitions (FIG 4). Thoracic radiographs supported spondylosis and scoliosis. A diagnosis of T11/T12 disc herniation was made. Patient declined discectomy and went for Ovearseas treatment

c) Case Reports 3

AA , a 72 year old male Nigerian has worsening chronic low back pain for 5 years with radiation to the lower limbs. He also had frequency , hesistancy , nocturia. normal Fasting blood sugar is normal and serum PSA was also norma (4 IU/L.). Abdomino-pelvic ultrasonography showed probably benign prostatic enlargement with volume of about 65mls. He has had bony fusion surgery as a result of a similar back pain 5years earlier. Lumbo-sacral spine radiograph showed L3/L4 bony ankylosis with L2/L3, L4/L5 disc space narrowing and spondylotic changes. Lumbo -sacral spine MRI showed bony fusion of L3/L4 with little residual anterior or posterior disc cartilage. L2/L3 and L4/L5 disc hernias were seen with L2/L3 severer than L4/L5. He had trans-urethral prostatectomy and conservative management of his multi-level disc hernias. He had post-operative urethral stricture complication in the penile –bulbous urethra which was bougeinaged.

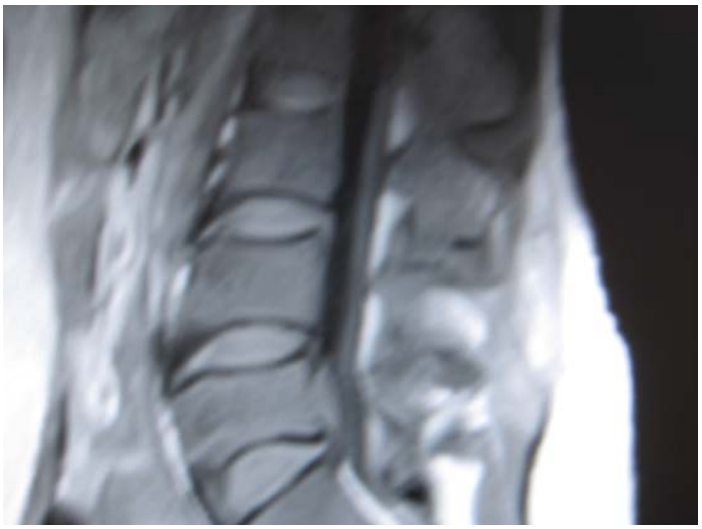


Fig .1 : Sagital T1w Mri Image Showing L4/L5 Sequestered Disc Hernia Behind L5

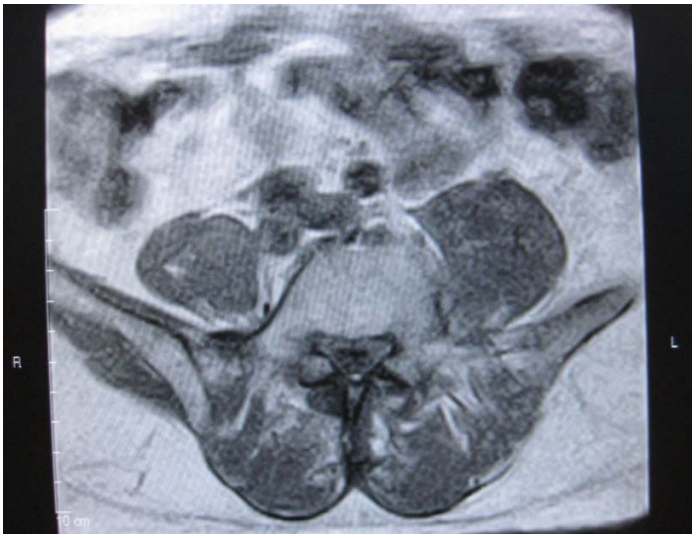


Fig. 2 : Axial T1w Mri Image Showing Sequesteredl4/L5 Herniated Disc In The Right of L5 Spinal Canal, Compressing Posterior Theca Sheath.

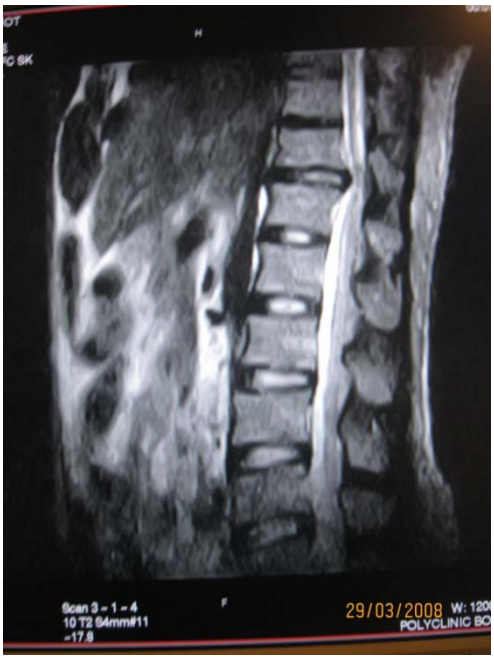


Fig. 3 : Sagital T2w Mri Image Showing Significant Anterior Theca Sheath Compression By T11/T12 Disc Hernia

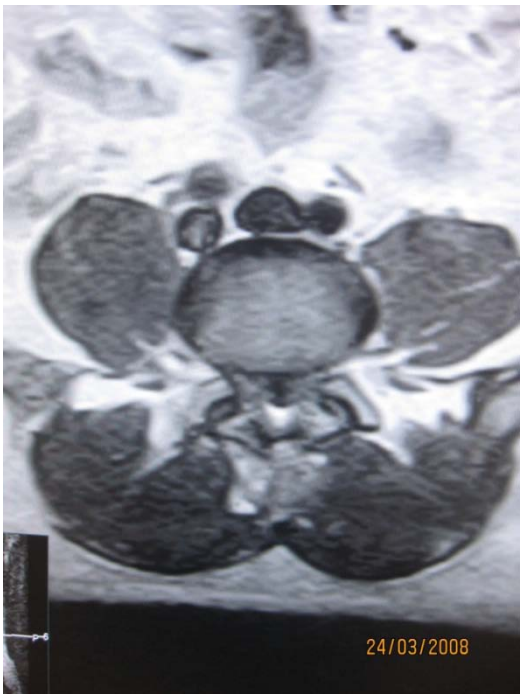
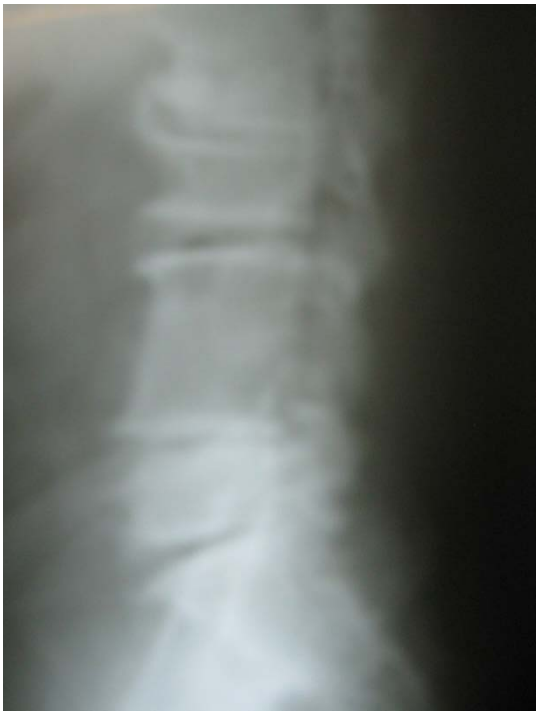


Fig. 4 : Axial Tiw Mri Image At T11/12 Showing Showing Bilateral Neural Foramina Narrowing, Worse On The Right



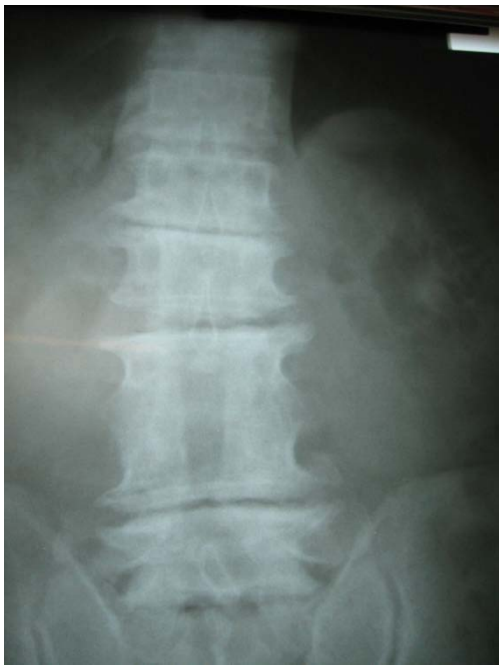


Fig. 5 and 6 : Lumbo - Sacral Radiograph Showing L3/L4 Bony Ankylosis. Intervening

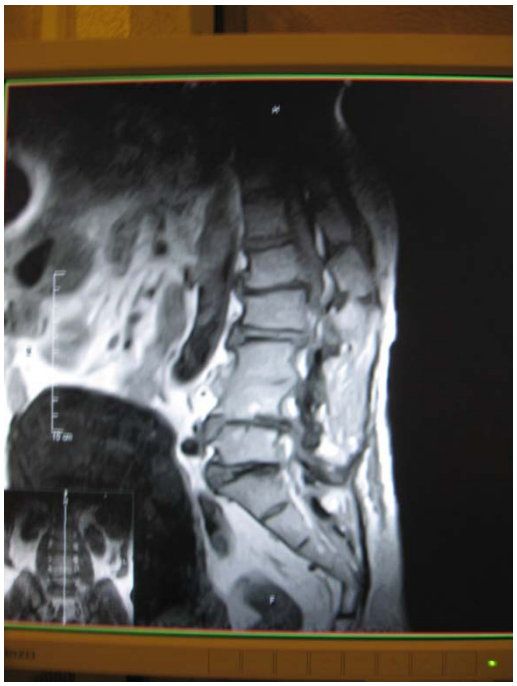


Fig. 7 : Intervening Residual L3/4 Disc Was Shown on MRI Image

III. Discussion

The 4 progressive phenomena in disc hernias are disc bulging, protusion or prolapse, disc extrusion and sequestration[8]. Disc bulging, according to description of Jansen is circumferential extension of the disc beyond the interface [9]. Annular bulge represents stretched but intact annular fibres and is usually asymptomatic except when canal is congentially narrow[9]. If there is now a focal tear of the inner margin of annulus , it is called disc protusion . When the tear is complete, it is called disc extrusion and the extruded disc is contained only by posterior longitudinal ligament. This disc can move cranially and caudad but it is always attached to parent disc. When this disc breaks loose from parent disc and not confined by posterior longitudinal ligament, it can either move superiorly or inferiorly , hence called disc sequestration [9] . When this free fragment lies near its parent disc , it's rounded in shape but irregular or oblong when separated from parent disc [10]. It may migrate to a different inter-space both in midline or in lateral recess, but can rarely penetrate the dura or cross the midline[10]. It is difficult to identify the posterior longitudinal ligament disruption [10] . MRI is the hallmark in the diagnosis of sequestrated disc (SD) due to its good soft tissue contrast and multi-planar nature [11] . The complementary use of Gado-pentetate Dimeglumine could obscure or clarify TIW and T2W MRI findings in such disc pathologies [11].

MRI radiological features of SD include Bull's eye sign of a rim enhancing round or oblong intra-spinal material isointense to parent disc [11]. The non-enhancing centre is regarded as a central dot sign [12]. The enhancing rim is due to inflammation and granulation tissue. Double fragment sign is the low signal intensity (dark line) between the SD and parent disc [12]. SD are easier to recognise in T2W and T2W* due to increased water content [10].

The signs and symptoms of SD are aggressive and severe. For example severe low back pains, lower limb pains and neurological deficits like cauda equine syndrome presenting with weakness of bladder and anal sphincters [13]. The pathogenesis of SD symptomatology is like any other disc herniation. Mechanical compression and inflammation in nerve root / dorsal root ganglia induced by herniated nucleus pulposus may play an important role in pathogenesis of spinal pain [7,14]. In the thoracic spine, the ratio of the diameter of the spinal cord to that of the spinal canal is large and the blood supply to this region is limited. This makes thoracic spinal cord vulnerable to compression from disc hernia [2] Herniated nucleus pulposus has even been thought as enchondroma arising from intervertebral disc producing nerve root compression [7]. It is also strongly considered that nucleus pulposus has inflammatogenic properties to affect the nerve root function, structure, vascular permeability and pain [7] . Such immunogenic potential is the current pathophysiological theory incriminating pro-inflammatory mediators produced on the surface of nucleus pulposus and causing nerve root pain [14,15]. Differential diagnosis of SD are Neurofibromatosis, Epidural abscess, Epidural fibrosis, Conjoined nerve roots (Tarlov cysts) and Wrapped disc [5,10].

The incidence of thoracic disc herniation is low compared to that of cervical or lumbar disc hernias. It constitutes only 1% of disc prolapse [16,17]. It actually represents 0.5% and 4.5% of all disc hernias [2] This is likely due to the unique anatomy and function of the thoracic spine [16,17]. Thoracic disc hernia is only 1% of disc prolapse with 75% of all thoracic hernia occurring below T8 and majority seen at T11/T12 [2,16,17] (as seen in our index patient). This is thought to be due to weakness of posterior longitudinal ligament and increased mobility of lower thoracic spine [2] Such T11/12 disc hernia was also reported by Isla et al who on surgical intervention even further revealed the hernia to be the rarer intra-dural thoracic disc herniation[18]. In the case of intra- dural disc herniation which forms only 0.26-0.30% of all herniated disc, thoracic type is greater (5%) than the cervical type which is 3% and lumbar taking 92% [19]. It is also most common in the 3rd and 4th decade of life like our own patient [16,17]. But middle age and older people are slightly more at risk if they indulge in strenuous activities. In terms of age incidence our index patient is similar to the case study of Sasaki et al who reported a rarer case of a thoracic

disc prolapsed at T2/T3 disc level [20] Thoracic disc is quite rare [3]. Upper thoracic disc hernia can mimmick cervical disc hernias whereas herniation of the rest of thoracic disc hernia can resemble lumbar disc hernia [3].

Thoracic disc injury occur spontaneously and risk factors for thoracic disc hernias are improper lifting, smoking, genetics, recreational activities, injury, pre existing degenerative changes [16,17,19]. Trauma is said to be a factor in only 10-20% of cases as noted in our patient [17].

The three major clinical presentation of thoracic disc herniation are axial pain, radiculopathy and myelopathy [21,22,25]. Axial pain with local compression of the surrounding anatomy causing thoracic back aches.Radiculopathy due to compression of passing nerve root leading to radiating pain along the rib cage and abdomenMyelopathy due to compression of the spinal cord leading to para pariesis of the legs, difficulty in walking, bowel and bladder control disorders. The pain could be midline, unilateral or bilateral and has an attendant radicular distributon [21,22,25]

Radiological investigations of disc hernias include, Computed tomography (CT) myelogram, Myelogram, Electromyelography,, Conventional radiography, and Nerve conduction velocity studies. The preferred modality of choice is Magnetic Resonance imaging (MRI) due to its multi-planar and good soft tissue contrast. With MRI, percentage spinal compromise by calculating mean canal cross-sectional area can be done, assisting in surgical prognostications [6].

The presence of a residual disc in between the fused L3/L4 vertebrae in the third case report supports acquired aetiology of spinal fussion (iatrogenic arthrodesis) instead of congenital vertebral segmentation anomaly.

Management of disc hernia could be conservative or surgical. The implication of chemical factors in patho-genesis of pain in disc hernia justifies conservative management [14]. This is supported by the fact that disc surgery does not consistently provide commensurate pain relief. Besides, large disc hernias are not always symptomatic and severe pain may be present in patients without any imaging evidence of nerve root compression. [14] Conservative therapy is often effective and considered as the severity of symptoms and neurological signs are often not well correlated with the size of disc hernias [14]. Methylprednisolone, Diclofenac,Indomethacin, Doxycycline and Cyclosporine may induce variable inhibition of this inflammatogenic effect [14,15]. Conservative management includes, rest, physical therapy, home exercise, hydrotherapy, epidural steroids, chiropractic manipulations and medications. This includes drugs like non-steroidal anti-inflammatory drugs, muscle relaxants like Carisoprodil, Benzodiazepine [17]. Herniated disc reabsorbs over time especially the larger uncontained extruded disc and SD[13] These types tend to regress even to a greater extent. [13].

Surgical treatment (Micro-discectomy) is done when conservative treatment fails. Surgical treatment is discectomy. This could be micro-surgical discectomy or minimally invasive endoscopic discectomy [20,25,26]. Minimally invasive micro-endoscopic discectomy causes less muscle injury than a traditional discectomy[26].Thoracic disc hernias represent only .15% and 1.8% of all surgically treated hernias [2].Transthoracic anterior-lateral route allows wide exposure for decompression [2]. In lateral approach to thoracic disc herniation , micro-surgery is done through a costo-transversectomy [22, 23]. Percutaneous micro-decompressive endoscopic thoracic discectomy with added application of non-ablative lower Holmium laser energy for disc shrinkage (laser thermodiskoplasty) appears to be easy, safe and efficacious. This less traumatic, easier outpatient treatment leads to excellent results, faster recovery and significant economic savings [24].

Patient after discectomy are able to return to normal job activity within 6 weeks [13]. McCulloch's judges functional outcome after discectomy into grade 1-4. Grade 1-is complete relief of symptoms , Grade 2 is mild discomfort and able to participate in all activities and grouped as satisfactory . Grade 3 - Is better than pre-operative status with significant limitations of activities and/or requiring medications and/or bracing. Grade 4 is unsatisfactory, no better than pre-operative status and unable to return to work [13]. Complications of discectomy exist. But a rare complication of recurrent radiculopathy resulting from epidural gas has been reported in 4 different cases [25].

Reoccurrence thoracic disc hernia is by proper lifting technique, good posture, dignity during standing and sitting, appropriate exercise, healthy weight and lean body mass, strengthened abdominal weak muscles, avoidance of smoking and positive attitude to stress.

IV. Conclusion

In conclusion,this is a further addition to literature documentations of uncommon types of disc hernias like thoracic disc hernia and sequestered disc hernia. Anticipation of further literature inputs will arise with increasing availability of MRI machines in developing world like Central African region.

The authors declare no conflict of interest.

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Mycological & Physico-Chemical Quality of Wheaten White Bread Flour Made for Nigerian Market

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Keywords : Mycological, physico-chemical, wheaten, flour, bread

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I. Introduction

Wheaten white bread flour consists mainly of ground endosperm of the wheat (*Triticum* species) kernel (Badshah *et al.,* 2005). There are several commercial grade of wheat flour and, the flour is made from different blends of wheat. The composition of the flour is therefore variable and the quality of the flour may differ according to geographical region, milling process, and the quality of the wheat (Quaglia, 1984).

Physico-chemical properties such as fat, carbohydrate, protein, moisture, ash, gluten and pH are of technological and nutritional importance. The proportion of these factors in the flour depends on the variety of wheat grain used and also depends on the standards recommended by the particular country's industrial standards (Adeyemi, 2003; Badshah *et al.,* 2005).

The standards for wheat flour (white flour) as recommended by Standards Organization of Nigeria (SON) and International Standards required that the flour be free from rancidity, objective odour, insects, rodents' hair and any other extraneous material (SON, 2000).

The quality of flour and storage condition after milling is very important in the shelf life of the flour. Studies have revealed that gradual changes of physico-chemical properties occur in the flour during storage (Kent-Jones and Amos, 1967; Sur *et al.,* 1993; Hruskova and Machova, 2002).

Mould growth has a detrimental effect on the quality of flour (Weidenborner *et al.,* 2000). A number of mould and yeast have been isolated from wheat flour and these fungi are responsible for the enzymatic activity in the flour. In a study in Germany, it was discovered that the overall degree of mould and mycotoxin contamination was lowered with decreasing ash content (Schollenberger *et al.,* 2002). This suggests a localization of the fungi primarily in the outer part of the wheat kernels. The recommendation for total mould count in Nigerian flour is 100 per gram of flour (SON, 2000).

There is very little or no information on the Mycological and Physico – chemical quality of flour in the Nigeria market. This survey is intended to augment the scarce information on the Mycogical and Physico – chemical quality of Nigeria flour.

II. Materials and Methods

a) Sample Collection

Freshly milled wheaten white flours ready for packaging were collected from four mills located at Lagos, Sapele, Ewu and Kano, all in Nigeria. Two samples were collected from each location in clean polythene bags and properly sealed. The samples were kept in the laboratory at room temperature and observed for bacteriological and physico – chemical changes. Samples were aseptically opened and analysed at 15 days intervals for a period of 4 months; this period was based on the assumed shelf – life of 3 – 4 months of the flour by the millers.

b) Mycological Analysis

The various types and numbers of mould and yeast associated with wheaten white bread flour were enumerated and quantified according to the method described by Harrigan and McCane (1976). Isolation of fungi was carried out using potato dextrose agar (PDA) (LABM) supplemented with chloramphenicol to inhibit

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bacterial growth. The media were incubated at 35°C for 72 hours. Total fungi were estimated as colony forming units per gram (cfu/g) of *flour.*

c) Characterization And Identification of Isolates

The fungi isolates were identified based on the examination of the conidial heads, phialides, conidiophores and presence or absence of foot cell or rhizoids (Samson and Reemon-Hoekstra, 1888). Wet preparations of actively growing fungi were placed on a glass slide with a methylene blue stain, covered with a cover slip and observed with X40 objective under the microscope.

d) Determination Of Physico – Chemical Properties of Flour

i. *pH*

A pH meter (JENWAY 3310) was used to determine the pH of 10% suspension of flour in water after standardizing with buffer at pH 7. A standard buffer 7 powder was prepared into 200ml solutions with distil and ionise in a volumetric flask. The buffer solution was poured into a beaker and the pH electrodes immersed in and regulated to stabilize at pH 7. There after, the electrodes were removed and introduced into the filtrate from the 10% flour suspension and allowed to stabilize and the final pH reading to be taken.

ii. *Moisture*

Moisture content was determined using the dry oven method (Polemeranz and Meloan, 1996).

iii. *Gluten*

Extraction of gluten was done according to the ICC (international cereal chemistry)– Standards No 106/1.

iv. *Protein*

Analysis of protein content was done using the Kjeldahl method. The sample was heated in sulphuric acid and digested until the carbon and hydrogen are oxidized and the protein nitrogen is reduced and transformed into ammonium sulphate. The concentrated sodium hydroxide is added and the digest heated (distillate) to drive off the liberated ammonia into a known volume of standard acid solution. The unreacted acid is determined and the results are transformed by calculation with factor 5.7 into a percentage of protein in the flour sample.

v. *Carbohydrate*

This was estimated according to the ICC – standard No. 123, method for the determination of starch content by hydrochloric acid dissolution.

vi. *Fat*

Extraction of fat was performed by the Soxtec method in automatic fat extraction unit using diethyl ether.

vii. *Ash*

Determination of flour ash was carried out according to the ICC – standards No. 104, for the determination of flour ash at 900°C. The difference in weight was used to estimate the crude ash; based on the moisture content of the flour, the ash on dry matter of the flour was calculated.

e) Statistical Analysis

Changes in bacteriological and physico – chemical qualities due to duration of storage for the different brands were analysed for statistical significance using the chi – square goodness of fit. Differences in the above qualities among the different flour brands were tested for statistical significance using the Single Factor Analysis of variance (ANOVA). Where significant differences were detected, the Duncan's Multiple Range (DMR) test was used to separate means on the basis of significance. All statistical tests were carried out using the ''SPSS10.0 package''.

f) Results

Average fungi counts for the brands of flour ranges from 3.357×10^3 cfu/g (Brand 4) to 10.144×10^3 cfu/g (Brand 1) (Table 10). Significant difference ($P = 3.153$) was recorded in fungi count flour brands. During storage, significant difference ($x^2 = 55.988$) was recorded for fungi count only in flour Brand 1, with day 0 having 27.65×10^3 cfu/g total fungal counts. Brands 2, 3 and 4 show no significant difference in fungal counts during storage (table 1). One yeast and five moulds were isolated (Table 2). The difference in the moisture content of the individual brands of flour is highly significant ($P = 21.966$) but there is no significant difference in moisture content of flour during storage. There was no significant difference ($P = 0.479$) in pH of individual flour. The pH ranges from 6.03 (brand 1) to 6.12 (brand 3) (table 10). Protein and gluten content of the individual flour shows highly significant difference ($P = 18.517$). Protein and gluten for brand 2 is 11.47% and 10.23% and for brand 4 is 10.24 and 8.64 respectively. Gluten content correlates with the protein content. Carbohydrate content was between 65 – 66% in all the brands of flour with no significant difference ($P = 0.248$). Ash content increases for the individual brands of flour during storage, but statistically, there is no significant difference (table 8).

However, there is a high significant difference ($P = 7.297$) in the ash of the different brands of flour with the range of 0.56% (brand 1) to 0.80%

(Brand 4) (Table 10). Fat content of the different brand of flour ranges from 0.92% (brand 3) to 0.98% (brand 4), no significant difference ($P = 0.915$) in the fat content of the various flour brands.

Table 1 : Total Fungal Count (Cfu/G X 10^3) Wheaten White Bread Flour During Storage

FLOUR BRANDS	STORAGE PERIODS								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	Significant
1	27.65 ± 0.0	4.5 ± 0.5	1.0 ± 0.0	3.0 ± 0.0	4.0 ± 0.0	13.5 ±0.5	13.5 ± 0.0	14.0 ± 0.0	P < 0.001
2	10.0 ± 0.0	7.5 ± 0.5	NO GROWTH	3.0 ± 0.0	6.5 ± 0.5	1.0 ± 0.0	2.0 ± 0.0	6.0 ± 0.0	P > 0.05
3	1.0 ± 0.0	9.0 ± 1.0	4.0 ± 0.0	3.5 ±0.5	3.5 ± 0.5	1.5 ± 0.5	2.5 ± 0.5	3.0 ± 1.0	P > 0.05
4	NO GROWTH	1.5 ± 0.5	3.0 ± 0.5	4.5 ± 0.5	4.5 ± 0.5	2.0 ± 0.0	1.5 ± 0.5	6.5 ± 0.5	P > 0.05

NOTE : P > 0.05 = not significantly different
P < 0.001 = highly significantly different

Table 2 : Fungi Associated With Whiten White Bread Flour During Storage

FUNGAL GROUP	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105
	BRANDS 1 2 3 4	BRANDS 1 2 3 4	BRANDS 1 2 3 4	BRANDS 1 2 3 4	BRANDS 1 2 3 4	BRANDS 1 2 3 4	BRANDS 1 2 3 4	BRANDS 1 2 3 4
Penicillium	+ ± ± ±	+ + + +	+ - ± ±	+ + + +	+ ± ±+	+ - - -	+ ± + +	+ + + +
Rhizopus	- - - -	- - - -	- - - -	- ± - -	± + ± -	- - - -	- ± + -	± + + ±
Mucor	- - - -	- - - -	- - - -	- - ± ±	- - - -	- - ± -	- - - -	- - - -
Odium	- - - -	- - - -	- - - -	- - - -	+ + - -	± + ± ±	- - - -	+ + - ±
Geotrichum	- - - -	- - - -	- ± ± +	- - - -	- - - -	- + - -	± ± - +	± + - ±
Saccharomyces	- - - -	- + - -	+ ± ± ±	+ - - -	- ± ± -	± - - -	- - ± -	- - -

+ = Present
± = Relatively present
- = Absent

Table 3 : Changes in Moisture Content (%) of Wheaten White Bread Flour During Storage

FLOUR BRANDS	MOISTURE CONTENT (%) AT								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	significant
1	12.92±0.02	12.85±0.01	12.48±0.37	12.26±0.06	12.92±0.05	13.03 ±0.00	13.16 ±0.06	12.97± 0.16	P > 0.05
2	13.00±0.06	12.67±0.04	12.53± 0.19	12.15± 0.01	12.79±0.02	12.98 ±0.09	13.00 ±0.01	13.00±0.01	P > 0.05
3	11.93±0.08	11.89±0.31	11.25± 0.05	11.60±0.44	12.02±0.05	12.27 ± 0.40	11.91±0.10	11.92±0.08	P > 0.05
4	13.65±0.08	13.23±0.01	13.19±0.01	13.22±0.02	13.71±0.03	13.82 ±0.13	13.80 ±0.07	13.85±0.00	P > 0.05

NOTE : P > 0.05 = not significantly different

Table 4 : Changes in Ph of Wheaten White Bread Flour During Storage

FLOUR BRANDS	pH OF FLOUR AT								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	significant
1	6.45±0.02	6.00±0.00	6.01 ±0.00	6.10 ± 0.05	5.76 ± 0.03	6.07 ± 0.15	6.20 ±0.01	5.64 ± 0.02	P > 0.05
2	6.20±0.01	6.01±0.01	6.01 ±0.01	6.14 ± 0.01	5.94 ± 0.01	6.14 ±0.04	6.18 ±0.01	5.77 ± 0.01	P > 0.05
3	6.21±0.01	6.03±0.01	6.0 ± 0.00	6.04 ±0.06	6.11 ± 0.01	6.21 ± 0.04	6.27 ±0.01	6.05 ± 0.03	P > 0.05
4	6.05±0.02	6.00±0.00	5.95 ±0.00	6.13± 0.01	6.09 ± 0.03	6.14 ±0.03	6.14 ±0.02	5.89 ± 0.08	P > 0.05

NOTE : P > 0.05 = not significantly different

Table 5 : Changes in Carbohydrate Content (%) of Wheaten White Bread Flour During Storage

FLOUR BRANDS	CARBOHYDRATE CONTENT (%) AT								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	significant
1	66.64 ±0.04	68.97 ±0.00	68.42 ±0.55	65.13 ±0.00	66.51 ±0.28	60.78 ± 2.21	62.65 ±0.15	64.33 ±0.03	P > 0.05
2	66.65 ±0.00	66.57 ±0.28	68.15 ±0.28	64.46 ±0.13	65.60 ±0.37	63.22 ±0.27	62.75 ±0.05	66.35 ±0.03	P > 0.05
3	60.40 ±0.20	67.97 ±0.10	68.15 ±0.28	65.78 ±0.10	69.20 ±0.27	62.95 ±0.55	63.75 ±0.25	68.70 ±0.20	P > 0.05
4	64.22 ±0.20	68.15 ±0.83	68.97 ±0.37	66.69 ±0.09	65.60 ±0.09	65.96 ±1.92	64.40 ± 0.20	66.30 ±0.10	P > 0.05

NOTE : P > 0.05 = not significantly different

Table 6 : Changes in Protein Content (%) of Wheaten White Bread Flour During Storage

FLOUR BRANDS	PROTEIN CONTENT (%) AT								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	significant
1	11.65 ±0.04	11.27 ± 0.03	11.55 ± 0.00	11.45 ± 0.05	11.49 ± 0.02	11.46 ± 0.06	11.44 ± 0.05	11.38 ± 0.02	P > 0.05
2	11.35 ±0.00	11.60 ± 0.07	11.64 ± 0.05	11.45 ± 0.03	11.45 ± 0.05	11.50 ± 0.02	11.34 ± 0.04	11.45 ± 0.05	P > 0.05
3	11.10 ±0.05	11.24 ± 0.13	11.41 ± 0.06	11.48 ± 0.08	11.18 ± 0.02	11.21 ± 0.01	10.98 ± 0.01	11.03 ± 0.02	P > 0.05
4	9.93 ± 0.08	10.09 ± 0.01	10.36 ± 0.01	10.12± 0.07	9.96 ± 0.04	10.02 ± 0.02	9.96 ± 0.02	9.85 ± 0.05	P > 0.05

NOTE : P > 0.05 = not significantly different

Table 7 : Changes in Gluten Content of Wheaten White Bread Flour During Storage

FLOUR BRANDS	GLUTEN CONTENT (%) AT								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	significant
1	10.40 ±0.00	9.96 ±0.05	10.00 ± 0.00	9.75 ± 0.15	9.68 ± 0.16	10.02 ±0.02	10.00 ± 0.00	9.90 ± 0.01	P > 0.05
2	10.05 ± 0.00	9.98 ± 0.02	10.02 ± 0.02	10.04 ± 0.00	10.28 ± 0.08	10.02 ± 0.02	10.01 ± 0.01	10.05 ± 0.05	P > 0.05
3	10.09 ± 0.06	9.95 ± 0.05	10.00 ± 0.00	10.10 ± 0.00	10.00 ± 0.02	10.25 ± 0.05	10.15 ± 0.05	9.98 ± 0.08	P > 0.05
4	8.94 ± 0.14	8.90 ± 0.15	8.75 ± 0.25	8.50 ± 0.00	8.55 ± 0.05	8.50 ± 0.00	8.55 ± 0.05	8.45 ± 0.05	P > 0.05

NOTE : P > 0.05 = not significantly different

Table 8 : Changes in Ash on Dry Matter Content of Wheaten White Bread Flour During Storage

FLOUR BRANDS	ASH ON DRY MATTER CONTENT (%) AT								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	significant
1	0.60 ± 0.00	0.61 ± 0.02	0.63 ± 0.01	0.64 ± 0.01	0.59 ± 0.02	0.62 ± 0.00	0.67 ± 0.01	0.67 ± 0.02	P > 0.05
2	0.50 ± 0.00	0.62 ± 0.00	0.65 ± 0.01	0.65 ± 0.01	0.60 ± 0.02	0.65 ± 0.02	0.69 ± 0.01	0.66 ± 0.01	P > 0.05
3	0.68 ± 0.02	0.69 ± 0.01	0.70 ± 0.00	0.73 ± 0.03	0.67 ± 0.03	0.71 ± 0.02	0.69 ± 0.01	0.71 ± 0.01	P > 0.05
4	0.74 ± 0.03	0.76 ± 0.03	0.79 ± 0.07	0.84 ± 0.04	0.78 ± 0.06	0.81 ± 0.04	0.83 ± 0.05	0.88 ± 0.03	P > 0.05

NOTE : P > 0.05 = not significantly different

Table 9 : Changes in Fat Content (%) of Wheaten White Bread Flour During Storage

FLOUR BRANDS	FAT CONTENT (%) AT								
	DAY 0	DAY 15	DAY 30	DAY 45	DAY 60	DAY 75	DAY 90	DAY 105	significant
1	0.92 ± 0.00	0.94 ± 0.04	0.93 ± 0.01	0.95 ± 0.01	1.08 ± 0.01	0.84 ± 0.03	0.92 ± 0.01	0.93 ± 0.01	P > 0.05
2	0.95 ± 0.01	1.04 ± 0.01	0.85 ± 0.01	0.87 ± 0.01	1.08 ± 0.02	0.95 ± 0.04	0.86 ± 0.01	0.88 ± 0.03	P > 0.05
3	1.07 ± 0.00	0.86 ± 0.04	0.83 ± 0.03	0.81 ± 0.01	1.05 ± 0.01	0.89 ± 0.06	1.02 ± 0.03	0.84 ± 0.02	P > 0.05
4	1.02 ± 0.02	0.95 ± 0.02	0.94 ± 0.03	0.94 ± 0.02	1.02 ± 0.02	1.02 ± 0.02	1.04 ± 0.01	0.94 ± 0.02	P > 0.05

NOTE : P > 0.05 = not significantly different

Table 10 : Average (*Ñ*) Summary on Quality Evaluation of Individual Brands of Flour

PARAMETERS	BRAND 1 *Ñ ± SD*	BRAND 2 *Ñ ± SD*	BRAND 3 *Ñ ± SD*	BRAND 4 *Ñ ± SD*	SIGNIFICANT
MOISTURE	12.82^{b} ± 0.11	12.77^{b} ± 0.31	11.97^{a} ± 0.58	13.56^{c} ± 0.29	P < 0.001
pH	6.03 ± 0.09	6.07 ± 0.04	6.12 ± 0.04	6.05 ± 0.03	P> 0.05
CARBOHYDRATE	65.31 ± 0.97	65.46 ± 0.65	65.87 ± 1.13	66.26 ± 1.12	P> 0.05
PROTEIN	11.46^{b} ± 0.04	11.47^{b} ± 0.04	11.09^{b} ± 0.15	10.24^{a} ± 0.11	P < 0.001
GLUTEN	9.96^{b} ± 0.08	10.23^{b} ± 0.37	10.28^{b} ± 0.48	8.64^{a} ± 0.19	P < 0.001
ASH	0.56^{a} ± 0.07	0.63^{b} ± 0.06	0.69^{c} ± 0.07	0.80^{c} ± 0.02	P < 0.001
FAT	0.94 ± 0.02	0.94 ± 0.03	0.92 ± 0.04	0.98 ± 0.11	P> 0.05
FUNGAL COUNT (X 10^{3}CFU/g)	10.14^{b} ± 3.13	4.50^{a} ± 1 24	3.50^{a} ± 0.87	3.36^{a} ± 0.71	P < 0.05

NOTE : Those with similar alphabet are not significantly different from each other.
P > 0.05 = not significantly different
P < 0.05 = significantly different
P < 0.001 = highly significantly different

III. Discussion

Total fungi counts of the flour during storage (Table 1) show no significant difference for only Brand 1 (x^2 = 55.988), but no significant difference was observed for the other flour Brands. Fungal counts from among the various Brands of flour show a significant difference (P = 3.153), flour Brand 1 has above 10_4 cfu/g and the other Brands below 5 × 10^3 cfu/g (Table 10).

Fungi thrive better at lower pH and this was reflected in the increase in the fungal counts at day 105 as the pH in all the flour Brands (Tables 1 and 4). Flour Brand 1 shows an increase in fungal count from 13.5 × 10^3 cfu/g 9day 90) to 14.0 × 10^3 cfu/g day 105) with a corresponding decrease in pH from 6.20 to 5.64. Corresponding in fungal counts were also observed in the other flour Brands (Tables 1 and 4). The increase in fungal counts for all the flour Brands at day 60 can be associated with the increase in moisture content of the flours. This finding is in agreement with the reports of Mashood *et al.* (2000) that mould growth in flour is favoured by high moisture content. *Penicillium* species was isolated throughout the storage period of the flour. This finding corresponds with previous studies that *Penicillium* species are among the dominant fungi in wheat and wheaten flour. Kent-Jones and Amos (1967) reported about 90% *Penicillium* of the total mould isolated from white flour and Weidenborner *et al.* (2000) also reported 15% *Penicillium* of the numerous mould counts (1.730 × 10^3 cfu/g) of white wheat flour.

Newer fungal groups begin to emerge as the storage progresses as a result of ecological succession with the yeast *Saccharomyces* being isolated at day 30 and 60 (Table 2). The isolation of yeast can be supported with increase in starch content at day 30 and 60. This finding correlates with previous report that yeast multiplication in flour occurs as a result of the high starch content (Kent-Jones and Amos, 1967). Other fungi such as the *Odium, Mucur, Geotrichum* were later isolated, this also is supported by previous studies that ecological succession occurs during storage of flour with *Penicillium* appearing after *Aspergillus* and followed later with *Mucur, Odium, Geotrichum* e.t.c. (Kent-Jones and Amos, 1967; Weidenborner *et al.,* 2000 and Schollenbeger *et al.,* 2002) a number of fungal species had been isolated from white wheat flour (Weidenborner *et al.,* 2000). Moulds usually contaminate the wheat from the field, despite the screening the wheat may pass through, the spores of the moulds cannot be completely eliminated since they are more resistant to heat and other chemicals. The effect can easily be observed after few days of storage of baked goods and even in the flour itself when left for long in the store. Mould growth usually produce undesirable odour in the flour products.

The increase in ash content of the flour may have encouraged proliferation of fungi. High ash content shows that there is much bran (the outer covering of the wheat grain) in the flour. This finding corresponds with the report of Schollenberger *et al.* (2002), that overall mould contamination was lower with decreasing ash content suggesting the localization of the fungi in the outer part of the wheat kernel. Total mould counts in all the flour Brands and during storage were above the standards of < 100 cfu/g (10^2 cfu/g) (Tables 1 and 10) recommended for Nigerian wheaten white flour (SON, 2000). Initially the ash contents for Brands 1 and 2 (Table 8) was within the acceptable limit value of < 0.65% (SON, 2000). Ash content however increased above the acceptable level for all the flours as from day 90 of storage. Flour Brands 3 and 4 have ash contents above 0.65 throughout the storage period (Table 8). There is however a significant difference in the ash content of the individual Brands of flour (P = 7.292) with flour Brands 1 and 2 having values of 0.56% and 0.63% respectively and Brands 3 and 4 of 0.69% and 0.80% respectively (Table 10).

The average fat content in the different brands flour shows no significant difference (P = 0.915) (Table 9). The value obtained for fat is acceptable as regarded <1.5% fat content for Nigerian white wheat flour (SON, 2000). Intermittent decrease was noticed in the protein content of the various brands of flour during storage. Flour brand 4 shows decrease in protein content from 10.02% (day 75) to 9.85% (day 105) and flour brand 2 shows a decrease in protein content from 11.64% (day 30) to 11.34% (day 90). The decrease noticed in the protein content of the flour corresponds with earlier reports that protein content flour decreases during storage (Sur *et al.,* 1993; Hruskova and Machova, 2002). The changes in protein content of the flour was however not significant, but average protein content for the individual brands of flour shows highly significant difference (P = 18.517) with brand 1 having 11.46% and brand 4; 10.24% (Table 10). Gluten content was seen to correlate with the total protein content as it also decreased slightly with storage (Table 6 and 7). This finding corresponds with previous reports of Sur *et al,* (1993) and Hrukova and Machova (2002).

IV. Conclusion

Wheaten white flour also referred to as the "all purpose" flour, because of unequal ability to produce gluten is used for several bakery products such as bread, pizzas, cakes and pastries, which are major supplements for breakfast. Wheat flour has high nutritional value, and hence is highly susceptible to spoilage. Fungi are primarily responsible for deterioration of grain especially when conditions of storage are favourable. This can be observed from the isolation of several moulds and yeast and the occurrence of ecological succession. There is therefore need to develop on methods to improve on and

preserve the quality of the flour for even longer period. This can be achieved by sourcing for high quality grade wheat and adequate monitoring and cleaning (screening) before milling. Good environmental hygiene practice and regular adequate cleaning of production lines will help to reduce wheat and flour contamination.

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25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. **Think technically:** Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be

sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page

- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

Title Page:

Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to

shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.
- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic

principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.

- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

Administration Rules Listed Before Submitting Your Research Paper to Global Journals Inc. (US)

Please carefully note down following rules and regulation before submitting your Research Paper to Global Journals Inc. (US):

Segment Draft and Final Research Paper: You have to strictly follow the template of research paper. If it is not done your paper may get rejected.

- The **major constraint** is that you must independently make all content, tables, graphs, and facts that are offered in the paper. You must write each part of the paper wholly on your own. The Peer-reviewers need to identify your own perceptive of the concepts in your own terms. NEVER extract straight from any foundation, and never rephrase someone else's analysis.

- Do not give permission to anyone else to "PROOFREAD" your manuscript.

- Methods to avoid Plagiarism is applied by us on every paper, if found guilty, you will be blacklisted by all of our collaborated research groups, your institution will be informed for this and strict legal actions will be taken immediately.)
- To guard yourself and others from possible illegal use please do not permit anyone right to use to your paper and files.

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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