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INFORMATION

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STATUS OF IODINE NUTRITION AMONG SCHOOL-AGE CHILDREN IN KARIMUI-NOMANE AND SINA-SINA YONGGOMUGL DISTRICTS IN SIMBU PROVINCE PAPUA NEW GUINEA

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ABSTRACT:
Iodine deficiency is regarded as the single most common cause of preventable mental impairment in communities with suboptimal intake of iodine. Universal Salt Iodization is the most effective and sustainable intervention strategy for prevention, control and elimination of iodine deficiency. Urinary iodine concentration is the biochemical indicator for assessing the iodine status of a population. This study was prompted by reports showing evidence of cretinism in Karimui-Nomane district in Simbu province. The major objectives were therefore to assess the availability of adequately iodized salt in households, the per capita discretionary intake of salt per day and the iodine status of school children (age 6 – 12 years) in Karimui-Nomane, the district of concern, and Sina Sina Yonggomugl, a comparison district in Simbu province. Iodine level was assessed in salt samples collected from randomly selected households in both districts. The head of each household completed a questionnaire on knowledge, attitudes and practices related to salt iodization. Urinary iodine concentrations were measured in spot urine samples collected from randomly selected 6 to 12 years old children from selected primary schools in the two districts. 82.4% and 63.8% of salt samples from Karimui-Nomane and Sina Sina Yonggomugl respectively were adequately iodized above the national standard of 30ppm. The mean per capita discretionary intake of salt in households in Karimui-Nomane district was 4.62 ± 0.42 g/day, and in Sina Sina Yonggomugl district was 6.0 ± 2.61g/day. At measured levels of iodization (mean iodine content 34.7ppm and 32.7ppm respectively), this amount of salt would provide the recommended intake of iodine (150ug/day). However, for children in Karimui-Nomane the median UIC was 17.5µg/L and the interquartile range (IQR) was 15.0 – 43.0µg/L. and in Sina Sina Yonggomugl, the median UIC was 57.5µg/L and the IQR was 26.3 – 103.0µg/L, indicating severe and mild iodine deficiency respectively. These apparently conflicting findings may be explained by the fact that only 34% of households in Karimui-Nomane and 72% of households in Sina Sina Yonggomugl had salt on the day of the survey. The results indicate that iodine deficiency is a significant public health problem in Karimui-Nomane and Sina Sina Yonggomugl districts in Simbu province, potentially because of lack of access to salt, rather than inadequate implementation of salt iodization. Further studies are needed to quantify access to salt for communities in areas that are not easily accessible like Karimui-Nomane district in Papua New Guinea and, if inadequate salt access is confirmed, to develop alternative or complementary strategies to salt iodization.

Keywords: School children, Iodine deficiency, Salt iodization, Urinary Iodine, Simbu province, Papua New Guinea
Submitted November 2017, Accepted December 2017

INTRODUCTION:

Suboptimal intake or low bioavailability of iodine can cause inadequate production of thyroid hormones, which are essential for normal growth and development [1, 2]. Iodine deficiency (ID) can lead to mental retardation in infants and children whose mothers were iodine deficient during pregnancy. ID is also regarded as the single most common cause of preventable mental impairment in communities with suboptimal intake of iodine [1, 2]. Marginal degree of ID can affect "apparently healthy" children – the manifestations may include poor performance in psychometric tests, and impaired mental and motor functions [1, 2]. ID is usually diagnosed across a target population and not specifically in an individual [2].

Universal salt iodization (USI) is the most effective intervention strategy for the control and elimination of ID [1 – 3]. The effective implementation of USI requires continuous monitoring of the process indicator, which is availability of adequately iodized salt in the households and the principal impact indicator, which is the iodine status, most commonly assessed by measuring iodine concentration of single urine samples from a representative sample of individuals in target populations [1, 3]. The sustainability of USI strategy can be assessed by combination of the median urinary iodine concentration (UIC) in the target population, the availability of adequately iodized salt at the households and a set of programmatic indicators that are regarded as evidence of sustainability [1, 2]. Due to wide variation in iodine excretion during the day and in between individuals, UIC cannot be used to assess iodine status of individuals. The median value of UICs in a population can however indicate population iodine status. As a result, median UICs cannot be used to assess the proportion of individuals with iodine deficiency or excess [1, 3].

USI was implemented in Papua New Guinea (PNG) in June 1995 with enactment of the PNG salt legislation, which prohibits the importation and sale of non-iodized salt [4, 5]. Reports from the PNG National Nutrition Survey in 2005 indicated that salt was adequately iodized in 92.5% of the households with salt and iodine status among non-pregnant women of child-bearing age was adequate in the four regions of PNG [6]. However, 38% of households had no salt at the time of the survey, and iodine status was lower in women from households without salt [6]. Meanwhile, several sub-national surveys carried out from 1998 to 2016 [7 – 14] indicated prevalence of mild to moderate iodine deficiency in some districts in PNG. However, no published data was available on the salt iodization and status of iodine nutrition in the Simbu province.

The current study was prompted by the report presented by the Chief Pediatrician in Simbu (Chimbu) Province during the midyear

consultative meeting of the Pediatric Society of PNG in 2014 [15]. The focus of the report was the nutritional status among infants and children in Karimui-Nomane district in Simbu Province. It included cases of cretinism and dwarfism diagnosed based on history taking and clinical examinations; several photographs of the children and family members were displayed. The diagnoses included Failure to Thrive (FTT), very low IQ, severe stunting, delay dentition, abdominal distention, umbilical hernia, unable to stand and walk and clinical evidence of hypothyroidism. The Chief Pediatrician also cited suspected cases of congenital hypothyroidism in the community. Most of the cases were cretins without goiter. Thus, because of lack of appropriate laboratory services, some of the diagnoses were confirmed by X-rays showing suspected characteristics of cretins.

Two of the X-rays showed delay in the development of the carpal bones in the wrist, delay in the development of bone centers of ossification indicative of congenital hypothyroidism, pronounced trabeculae in the structure of the metaphyses in the distal end of the femur and the proximal end of the tibia. The Femoral head center of ossification shows traces (Figs 1 and 2).

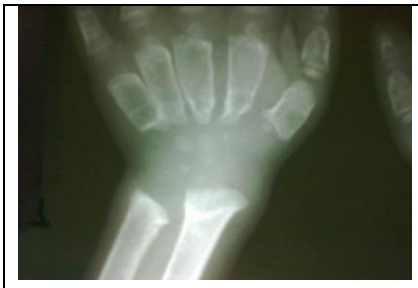

Fig. 1: X-ray of carpal bones in the wrist [15]

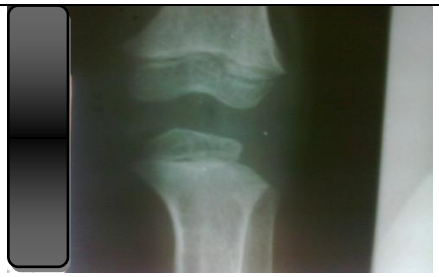

Fig. 2: X-ray of distal end of femur and proximal end of tibia [15]

These X-rays are similar to those of patients with hypothyroidism [16, 17].

The report further stated that in Karimui-Nomane district there is a salt water stream that flows out from rocks. The salt water was used to flavour foods by the forefathers of the land, the neighbouring tribes and the whole of Simbu province. Local history indicated that it was a great commodity in the past. It was used in exchange for other goods / items and even for bride price payments [15]. A similar report was presented during the midyear consultative meeting in 2015 because of concerns that no action had been taken [15].

The conclusion of both reports was "*an apparently very high prevalence of probably severe iodine deficiency disorders (IDD) exists*

among the population in Karimui-Nomane district, which is one of the remote districts in the Simbu province". An urgent plea was made for appropriate scientific investigations to be carried out in the district followed by appropriate actions.

The major objectives of this study were therefore to assess the availability of adequately iodized salt in households, the per capita discretionary intake of salt per day and the iodine status of school children (age 6 – 12 years) in Karimui-Nomane and Sina-Sina Yonggomugl districts in Simbu province.

SUBJECTS AND METHODS:

Study sites:

This study was conducted in the Simbu (Chimbu) province located in the highlands region in PNG. The province has an area of 6,112 Km^2 with a population of about 376,473. It shares geographic and political boundaries with five other provinces: Southern Highland, Jiwaka, Eastern Highland, Gulf and Madang. Simbu is a province with very rugged mountainous terrains, including the tallest mountain in PNG, Mt. Wilhelm, and other notable mountains, like Mt. Elimbari, Mt. Digine, and Mt. Crater [18]. The annual rainfall varies between 4,855 mm at high altitudes to 1,599 mm at lower altitudes. There are six districts in Simbu province: Chuave, Gumine, Karimui-Nomane, Kerowagi, Kundiawa-Gimbogi and Sina Sina-Yonggomugl. The provincial capital is Kundiawa, which is located in Kundiawa-Gimbogi district.

The specific sites for the study were Karimui-Nomane and Sina Sina Yonggomugl districts. Sina Sina Yonggomugl district was assessed in addition to Karimui-Nomane as a comparison as it is less remote and mountainous and closer to the capital city [18].

Sample size for assay of urinary iodine concentration:

Calculation of sample size used a design effect of three, a relative precision of 10%, and confidence level (CL) of 95% [19]. As there was very limited information on likely prevalence rates of ID in both provinces, an assumed prevalence rate of 25% was used for each district. With a predicted non-response rate of 10%, the sample sizes of 300 and 250 school-age children were obtained for Karimui-Nomane and Sina Sina Yonggomugl districts respectively. These sample sizes were considered adequate for a mini-survey with limited resources and also because of the lack of recent data on the status of iodine nutrition among in the population in these districts and this province.

Study design and sampling:

This was a prospective school and community based cross-sectional study. The study population included 6 to 12 years old school children randomly selected from all of the primary

schools in the two districts; seven in Karimui-Nomane and three in Sina Sina Yonggomugl. Multistage cluster sampling method was used in both districts. The total enrolments in each of the selected primary schools, including the ages of children in each of the grades were listed. The required number of children from each of the primary schools in each district was selected by simple random sampling.

Salt samples were collected from randomly selected households in Karimui-Nomane and Sina Sina Yonggomugl districts. The head of each household was also requested to complete a questionnaire. The pre-tested questionnaire was used to assess the awareness and use of iodized salt in the households in both districts.

Collection of samples and questionnaires:
The major objectives of the study were explained to the head of each school and to the teachers, requesting them to communicate the information to the parents. Single urine samples were collected at the school from each of the selected school children, after obtaining informed consent from their parents or guardian. Each urine sample was kept in a properly labelled sterile plastic tube with tight fitting stopper that was further sealed with special plastic bands.

To assess the availability of salt, households were randomly selected from a list of households in both districts. For households with salt available at the time of the survey, a teaspoon of salt was collected from the salt available in each household and placed in a labeled zip-locked bag.

To determine the discretionary intake of salt, sealed packets containing 250g of iodized table salt were distributed to 50 randomly selected households in each district. The number of individuals living in each household and eating food prepared in the household was counted and recorded. The head of the household was requested to use the salt as usual for cooking and eating. Each household was visited a second time a few days later to determine the amount of salt remaining in the packet. The number of individuals living in each household was again counted and recorded. The data obtained was used to estimate the average discretionary intake of salt per capita per day for each district.

Two clean properly labelled sterile containers were used to collect water from the salt stream in Karimui-Nomane district.

The completed questionnaires were also collected from the various households. The salt samples, urine samples and questionnaires were appropriately packed into suitable containers and transported by airfreight to the Micronutrient Research Laboratory (MNRL) in the School of Medicine and Health Sciences (SMHS)

University of Papua New Guinea (UPNG) for analyses.

Exclusion criteria:

All children below 6 years of age and above 12 years of age were excluded from the study. Urine samples were collected only from children whose parents or guardians gave consent.

Analysis of samples:

The iodine content in the salt samples and the water from the salt stream were determined quantitatively using the WYD Iodine Checker [20]. Internal bench quality control (QC) for daily routine monitoring of performance characteristics of the WYD Iodine Checker was by the Westgard Rules using Levy-Jennings Charts. The percent coefficient of variation (CV) ranges from 2.5% to 5.0% throughout the analysis.

The UIC was determined by Sandell-Kolthoff reaction after digesting the urine with ammonium persulfate in a water–bath at 100°C [1].

Internal bench QC characterization of the assay method was by the Levy-Jennings Charts and the Westgard Rules. In addition, the sensitivity (10.0 – 12.50µg/L) and percentage recovery (95.0 ± 10.0%) of the urinary iodine (UI) assay were frequently used to assess the performance characteristics of the assay method. External QC monitoring of the assay procedure was by Ensuring the Quality of Urinary Iodine Procedures (EQUIP), which is the External Quality Assurance Program (QAP) of the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA.

Data analysis and Interpretation:

Microsoft Excel Data Pack 2010 and the Statistical Package for Social Sciences (SPSS) software (version 17) were used for statistical analyses of the data. Shapiro-Wilks test was used to assess normality of the data. Mann Whitney U test was used for differences between two groups; Kruskal-Wallis and Friedman were used for comparison of all groups. Analysis of variance (ANOVA) was also used to compare differences between groups. Scheffe test was used for post-hoc analysis. $P < 0.05$ was considered as statistically significant.

The PNG salt legislation was the criteria used for interpretation of the iodine content in salt samples. According to the legislation all salt must be iodized with potassium iodate; the amount of iodine in table salt should be 40 – 70ppm (mg/kg); the amount of iodine in other salt should be 30 – 50ppm. This implies that the iodine content in salt at the time of consumption should not be less than 30ppm [4, 5].

The recommended WHO/UNICEF/ICCIDD criteria [1] for the interpretation of UIC data were used to characterize the status of iodine nutrition among the school children in Karimui-Nomane and Sina Sina Yonggomugl districts. According to

the criteria, a population of school-age children is considered iodine deficient if the median UIC is below 100µg/L and iodine sufficient if the median is in the range of 100-200µg/L. In addition, not more than 20% of the urine samples should be below 50µg/L in an iodine sufficient population. The median UIC can also be used to indicate the severity of deficiency, for example a population with median UIC <20µg/L is considered severely deficient and moderately deficient if it is 20-49µg/L [1].

Ethical Clearance:

Ethical clearance and approval for this study were obtained from the SMHS Ethics and Research Grant Committee and PNG Medical Research Advisory Committee (PNG MRAC). Permission was obtained from the appropriate authorities in Simbu Province, Karimui-Nomane district, Sina Sina Yonggomugl district, the authorities in the various schools, heads of households and the parents of the selected children.

RESULTS:

Questionnaires:

A total of 67 households completed the questionnaires in Karimui-Nomane district compared to 25 households in Sina Sina Yonggomugl district. Of the 67 participants that completed the questionnaires in Karimui-Nomane district, 64.2% (43/67) were males and 35.8 % (24/67) were females. The mean age of the 67 participants was 38.0 ±14.2 years, age range was 16.0 to 70.0 years and median age was 36.0 years. For their level of education, 43.3% (29/67) had secondary school education, 37.3% (25/67) completed university, 16.4% (11/67) completed primary school and 3.0% (2/67) could not read or write. A total of 98.5% (66/67) of the participants were married and 1.5% (1/66) was single. For their employment status, 95.5% (64/67) were unemployed and 4.5% (3/67) were employed. One of the major reasons for the low employment rate is because of the remoteness of the district.

The participants in Sina Sina Yonggomugl were comparable except many more were female and less were married. The mean age of all the 25 participants in Sina Sina Yonggomugl was 37.7 ± 13.3 years, age range was 21.0 to 78.0 years and median age was 35.0 years. There were 7 (28.0%) male and 18 (72.0%) female participants. 52.0% (13/25) of the participants had primary school level education, 36.0% (9/25) had secondary school level education and 12.0% (3/25) completed university. For marital status, 76.0% (19/25) were married, 16.0% (4/25) were single and 8.0% (2/25) were widows. All the 25 participants were unemployed. No specific reasons could be given for the low employment rate.

Knowledge, awareness and practices related to the use of iodized salt:

The participants in the 67 households in Karimui-Nomane and the 25 households in Sina Sina

Yonggomugl districts stated yes to the question "Do you use salt at home?" In Karimui-Nomane 14.9% (10/67) used the salt for cooking only, and 85.1% (57/67) use salt for cooking and adding to food before eating.

When asked if they use iodized salt at home, 52.2% (35/67) were positive that they use iodized salt at home, 1.5% (1/67) said they do not use iodized salt at home and 46.3% (31/67) was not sure. 77.6% (52/67) had no knowledge about why it is important to use iodized salt. 34.3% (23/67) said they always purchase salt from the local markets, 58.2% (39/67) purchase salt from the supermarkets, and 7.5% (5/67) purchase from the local markets and trade stores.

When asked how often they eat food from the sea, 17.9% (12/67) said frequently, 58.2% (39/67) said once in a while and 23.9% (16/67) admitted that they have never consumed food from the sea. None of the participants responded to the question regarding the use of traditional salt, including water from the salt stream.

In Sina Sina Yonggomugl district 16.0% (4/25) used the salt for cooking only, and 84.0% (21/25) use salt for cooking and adding to food before eating.

When asked if they use iodized salt at home, 92.0% (23/25) were positive that they use iodized salt at home, 4.0% (1/25) said they do not use iodized salt at home and 4.0% (1/25) was not sure if they use iodized salt at home. 88.0% (22/25) had no knowledge about the use of iodized salt. 36.0% (9/25) said they always purchase salt from the local markets and 64.0% (16/25) purchase salt from the supermarkets and other shops.

When asked how often they eat food from the sea, all the participants (100%) admitted that they have never consumed food from the sea. The participants did not respond to the question about the use of traditional salt at home.

Salt Consumption and Iodization (**process indicator**):

Availability of salt in households:

In each district 50 households participated in this section of the study. Each household was visited twice. At the time of the first visit salt was available in 17 (34.0%) of the 50 households in Karimui-Nomane district, and in 36 (72.0%) of the 50 households in Sina Sina Yonggomugl district. A teaspoon of salt was collected from each household where salt was available.

Iodine content in salt from the households:

The summary statistics of the iodine content (ppm) in the salt samples collected from the households are presented in Table 1.

The mean (± STD) iodine content in salt samples from households in Karimui-Nomane was 34.7 ± 13.4ppm and the range was 1.9 – 64.7ppm; for salt samples from Sina-Sina Yonggomugl the mean iodine content was 32.7 ± 10.5ppm and the range was 2.0 – 62.6ppm.

The Iodine content was below 30.0ppm in 3 (17.6%) of the 17 salt samples from households in Karimui-Nomane and 13 (36.2%) of the 36 salt samples from households in Sina-Sina Yonggomugl districts indicating that 82.4% and 63.8% of households with salt at the time of the survey in Karimui-Nomane and Sina-Sina Yonggomugl districts had adequately iodized salt. In both districts, the iodine content in was below 15ppm in only one sample.

Iodine content in water from salt stream in Karimui-Nomane district:

The iodine content was zero in the two water samples collected from the salt water stream in Karimui-Nomane district at the time of this study.

Table 1: Summary statistics of Iodine content (ppm) in salt samples collected from the households in the two districts

Parameters	Karimui-Nomane	Sina Sina Yonggomugl
Salt available	17 (34%)	36 (72%)
Mean (ppm)	34.7	32.7
Std Dev (STD)	13.4	10.5
95% Confidence Interval (95% CI) (ppm)	27.8 – 41.6	29.2 – 36.3
Range (ppm)	1.9 – 64.7	2.0 – 62.6
Median (ppm)	33.5	33.0
Interquartile Range (IQR)	30.7 – 39.9	27.4 – 36.9
Number (%) of salt with Iodine content<30ppm	3 (17.6%)	13 (36.2%)
Number (%) of salt with Iodine content ≥30ppm	14 (82.4%)	23 (63.8%)
Number (%) of salt with iodine content <15ppm	1 (5.9%)	1 (2.8%)

Table 2: Summary statistics of the discretionary intake of salt per capita per day in both districts

Parameters	Karimui-Nomane	Sina Sina Yonggomugl
N	47	39
Mean (g)	4.62	6.0
Standard Deviation (STD)	0.42	2.61
95% Confidence Interval (95% CI) (g)	3.78 – 5.48	5.15 – 6.85
Range (g)	0.30 – 14.20	1.6 – 11.9
Median (g)	3.80	5.80
Interquartile Range (IQR) (g)	2.80 – 6.75	4.1 – 7.75

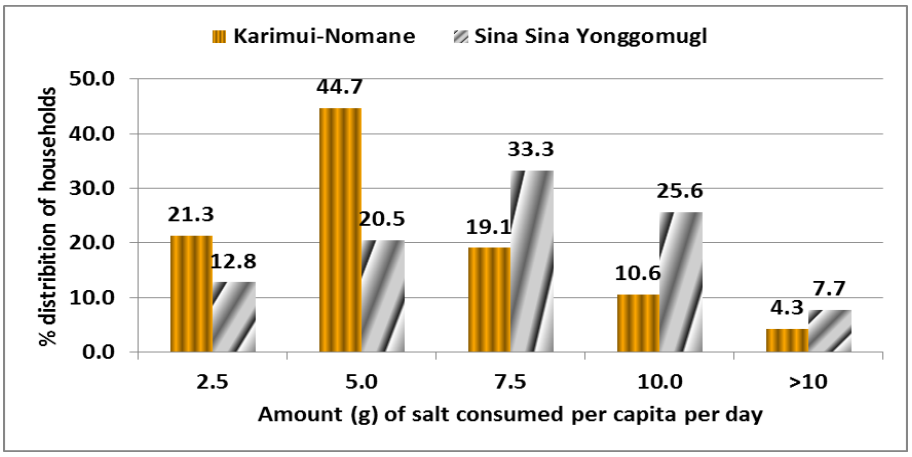

Fig. 2: Frequency (%) distribution of the per capita discretionary intake of salt per day in households in Karimui-Nomane and Sina Sina Yonggomugl districts

Discretionary intake of salt per capita per day:

The summary statistics of the discretionary intake of salt per capita per day in Karimui-Nomane and Sina Sina Yonggomugl districts are presented in Table 2. While 50 households in each district were given a package of salt in order to assess discretionary intake, only 47 households from Karimui-Nomane and 39 from Sina Sina Yonggomugl gave permission for the package to be weighed at the time of the second visit. In Karimui-Nomane district the mean per capita discretionary intake of salt was 4.62 ± 0.42 g/day and the range was 0.3 – 14.2 g/day. In Sina Sina Yonggomugl district the Mean was 6.0 ± 2.61g/day and range was 1.6 – 11.9 g/day. The Mann-Whitney U and Wilcoxon W tests indicate statistically significant difference (p = 0.01. two-tailed) between the discretionary daily per capita intake of salt in households in Karimui-Nomane district compared to Sina Sina Yonggomugl district. Similar results were obtained using the Kruskal Wallis and Chi-Square tests (p = 0.011).

The frequency distributions of the discretionary per capita consumption of salt per day in households in Karimui-Nomane and Sina Sina Yonggomugl districts are presented in Fig. 2. In Karimui-Nomane district the discretionary consumption of salt per capita per day was up to 5.0g in 66.0% (31/47) of the households compared to 34.0% (16/47) consuming over 5.0g of salt. This was in contrast to the results for households in Sina Sina Yonggomugl where 33.3% (13/39) of the households were consuming up to 5.0g of salt per capita per day compared to 66.7% (26/39) consuming over 5.0g of salt.

Estimated intake of iodine per capita per day:

The mean discretionary intake of salt per capita per day in households in Karimui-Nomane district was 4.62 ± 0.42g. The mean iodine content in the salt from the households was 34.7 ± 13.4ppm. Thus, the calculated mean

discretionary intake of iodine per capita per day was 160.3 ± 14.6µg. Assuming that 20.0% of iodine in the salt was lost during storage and food preparation, the calculated per capita discretionary intake of iodine was 128.2 ± 11.7µg per day.

For households in Sina Sina Yonggomugl district, the mean discretionary intake of salt was 6.0 ± 2.61g; the mean iodine content in salt was 32.7 ± 10.5ppm. The calculated mean discretionary intake of iodine per capita per day was 196.2 ± 85.3µg per day. Assuming 20.0% of iodine was lost in the salt during storage and food preparation, the calculated per capita discretionary intake of iodine was 157.0 ± 68.2µg per day.

URINARY IODINE CONCENTRATION (impact indicator):

For the assessment of iodine status, 301 children were randomly selected from 7 schools in Karimui-Nomane district and 261 children from 3 schools in Sina Sina Yonggomugl district. Casual urine samples were collected from 293 children in Karimui-Nomane and 252 children in Sina Sina Yonggomugl districts. These gave non-response rates of 2.7% in Karimui-Nomane and 3.4% in Sina Sina Yonggomugl districts.

The distributions of the UIC for the 291 children in Karimui-Nomane and 253 children in Sina Sina Yonggomugl are presented in the Box-plots in Fig 3. The Box-plots show that the UIC (µg/L) data were not normally distributed. This was confirmed by the Shapiro-Wilks tests (p = 0.001) for normality of distribution. Thus, non-parametric statistics were used for further analysis of the UIC data.

The summary statistics of the UIC (µg/L) for the 291 and 253 children in Karimui-Nomane and Sina Sina Yonggomugl districts respectively are presented in Table 3. For children in Karimui-Nomane the median UIC was 17.5µg/L and the interquartile range (IQR) was 15.0 – 43.0µg/L. In addition, 97.3% (283/291) of the children had UIC less than 100.0µg/L and 77.7% (226/291) had UIC below 50.0µg/L.

For the children in Sina Sina Yonggomugl, the median UIC was 57.5µg/L and the IQR was 26.3 – 103.0µg/L. 73.1% (185/253) had UIC below 100.0µg/L and 41.5% (105/253) had UIC below 50.0µg/L.

The Mann-Whitney U and Wilcoxon W tests indicated statistically significant difference (p = 0.001, 2-tailed, Z = - 9.847) between the UIC of the children in the two districts. This was further confirmed by the Kruskal Wallis and Chi-Square tests (p = 0.001).

The median UIC values of 17.5ug/L and 57.5ug/L for the children in Karimui-Nomane and Sina Sina Yonggomugl districts indicate severe and mild iodine deficiency respectively.

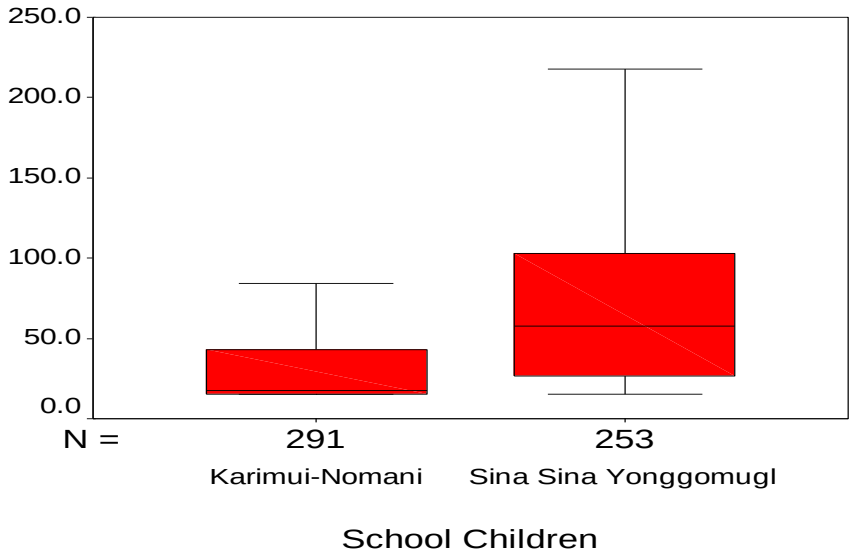

Fig. 3: Box-plots of urinary iodine concentrations (µg/L) in school children from Karimui-Nomane and Sina Sina Yonggomugl districts

Table 3: Summary statistics of urinary iodine concentration (µg/L) for the school children in Karimui-Nomane and Sina Sina Yonggomugl districts

	Karimui-Nomane	**Sina Sina Yonggomugl**
Parameters	**All children (n = 291)**	**All children (n = 253)**
Median (µg/L)	**17.5**	**57.5**
IQR (µg/L)	**15.0 – 43.0**	**26.0 – 103.0**
Mean (µg/L)	33.1	72.5
Std Dev	27.2	83.3
95% CI (µg/L)	29.9 – 36.2	62.2 – 82.8
Range (µg/L)	15.0 – 135.5	15.0 - 217
Percent (n) of children with UIC< 100µg/L	**97.3% (283)**	**73.1% (185)**
Percent (n) of children with UIC< 50µg /L	**77.7% (226)**	**41.5% (105)**

For further analyses of the UIC data the children were separated according to gender. Gender was not indicated in 8 (2.7%) of the 291 urine samples from Karimui-Nomane district and in 9 (3.6%) of the 253 urine samples from Sina Sina Yonggomugl district. Of the urine samples from Karimui-Nomane, 55.8% (158/283) were from male and 44.2% (125/283) from female children. For urine samples from Sina Sina Yonggomugl district 56.6% (138/244) from male and 43.4% (106/244) from female children.

Fig 4 show the Box-plots for the UIC (µg/L) obtained for the male and female children in both

districts. The results indicate that the UIC were not normally distributed, which were confirmed by the Shapiro-Wilks tests for normality of distribution (p = 0.001).

The summary statistics of the UIC (µg/L) for the male and female children in Karimui-Nomane and Sina Sina Yonggomugl districts are presented in Table 4. The median UIC for the male and female children in Karimui-Nomane district was 16.5µg/L and 15.5µg/L respectively; the IQR for the male children (15.0 – 42.0µg/L) was similar to that of female children (15.0 – 42.0µg/L). There was no statistically significant difference (p = 0.751, 2-tailed) between the UIC for the male and female children in Karimui-Nomane district.

For the male children in Sina Sina Yonggomugl, the median UIC was 61.3µg/L and the IQR was 25.1 – 108.1µg/L; for the female children, the median was 53.5µg/L and IQR was 26.3 – 93.6 µg/L. The UIC for the male children was not significant different (p=0.182, 2-tailied) from those of the female children.

The UIC for the male and female children in Karimui-Nomane district were significantly lower than the UIC for the male (p = 0.001, 2-tailed) and female (p = 0.001, 2-tailed) children in Sina Sina Yonggomugl district.

Fig. 4: Box-plots of UIC for male and female school children in Karimui-Nomane and Sina Sina Yonggomugl districts Simbu Province

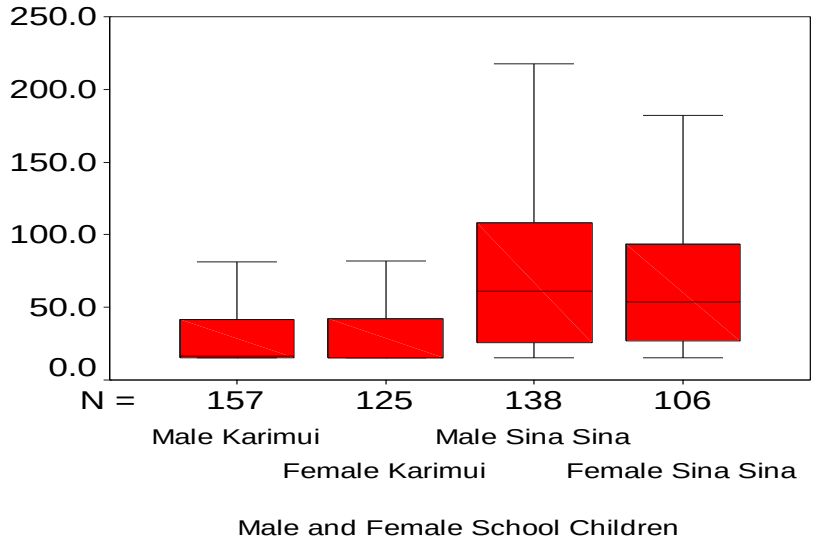

Table 4: Summary statistics of the UIC (µg/L) for the male and female school children in Karimui-Nomane and Sina Sina Yonggomugl districts

	Karimui-Nomane		Sina Sina Yonggomugl	
Parameters	**Male children (n =158)**	**Female children (n = 125)**	**Male children (n = 138)**	**Female children (n = 106)**
Median (µg/L)	**16.5**	**15.5**	**61.3**	**53.5**
Interquartile Range (IQR) (µg/L)	**15.0 – 42.0**	**15.0 – 42.0**	**25.1 – 108.1**	**26.3 – 93.6**
Mean (µg/L)	32.3	32.9	81.0	63.1
Std Dev	26.0	28.4	105.1	44.0
95% CI (µg/L)	28.2 – 36.4	27.9 – 37.9	63.3 – 98.7	54.7 – 71.6
Range (µg/L)	15.0 – 135.5	15.0 – 132.0	15.0 – 217.5	15.0 – 182.0
Percent (n) of children with UIC below 100µg/L	**97.5% (154)**	**96.8% (121)**	**67.4% (93)**	**81.1% (86)**
Percent (n) of children with UIC below 50µg/L	**77.8% (123)**	**80.0% (100)**	**37.0% (51)**	**45.3% (48)**

For the male and female children in Karimui-Nomane district, median UIC of 16.5µg/L and 15.5µg/L respectively indicate severe iodine deficiency and insufficient intake of iodine. For the male and female children in Sina Sina Yonggomugl district, median UIC of 61.3µg/L and 53.5µg/L respectively indicate mild status iodine deficiency and insufficient intake of iodine.

DISCUSSION:

All the participants in both districts that completed the questionnaires stated that "they use salt at home", supporting the global norm that everyone eats salt, and premise of the salt iodization strategy that salt is a good vehicle for iodine fortification. However, when asked if salt was available, only 34% said 'yes' in Karimui-Nomane and only 72% in Sina Sina Yonggomugl. This is much lower than the global norm and may indicate that salt is less appropriate as a fortification vehicle in some areas of PNG. Use of salt may be low in some areas of PNG because availability of commercial salt is constrained by remoteness and distance from ports, as the majority of salt is imported, and/or because of the availability of "traditional salt" such as the salt stream reported in Karimui-Nomane district. According to anecdotal reports, in some areas in Karimui-Nomane district, two practices are used; water from the salt stream is sprinkled on food for taste or grass is soaked in the water from the salt stream then allowed to dry before being incinerated and the ash used as salt on foods.

In households where salt was available however, almost all was iodized above 15ppm (94.1% and 97.2% in Karimui-Nomane and Sina Sina Yonggomugl respectively), and the majority was iodized above 30ppm, the national standard (82.4% and 63.8% respectively). Other studies in PNG have found similar high rates of adequate salt iodization in households; 95.0% in Hela

district in 2004 [8], 94.5% in National Capital District (NCD) in 2006 [10], 95.0% in NCD in 2009 [11] and 78.0% in Morobe and Eastern Highlands Provinces in 2013 [12].

This study found discretionary salt intake to be relatively low in the two districts studied, at around 5g per capita per day, compared to an estimated global average of 10.06g [21]. Moreover, this study's estimate might be an over-estimation as it is based on the amount of salt consumed from packages provide free to the households during the survey. It is possible that the households may have consumed more than they normally would when they have to purchase the salt themselves. However, studies in other parts of PNG have also recorded relatively low and even lower salt consumption; 6.59g in Lae city, Morobe province [7]; 2.62g in Hela province [8]; and 4.7g in Morobe and Eastern Highlands provinces [12]. Nevertheless, despite the low discretionary salt intake in PNG, at current levels of iodization, it would provide sufficient amount of iodine of 150ug/person/day [1] to prevent deficiency and salt iodization would be expected to be highly effective.

However, salt with iodine content above 30ppm was available in only 28.0% (14/50) and 46.0% (23/50) of selected households in Karimui-Nomane and Sina Sina Yonggomugl districts respectively. Thus, according to the PNG salt legislation only 28.0% and 46.0% of randomly selected households in Karimui-Nomane and Sina Sina Yonggomugl districts respectively had adequately iodized salt at the time of this study [4, 5]. These values are lower than the 90.0% recommended coverage of households with adequately iodized salt that should indicate effective implementation of the USI strategy in PNG.

Our data indicate that salt iodization is unlikely to be effective in these two districts in Simbu province, and indeed, school age children in both districts were found to be iodine deficient. Unlike in other countries where salt iodization levels and even non-iodization is the limiting factor to effectiveness of salt iodization, in PNG availability of salt may be the limiting factor. Data on salt availability in PNG is limited. As already reported, 38% of households sampled for the National Nutrition Survey of 2005 had no salt on the day of the data collection; this proportion was as high as 50% in the Southern region and between 32% and 36% in the remaining regions; it was 42% in rural areas [6]. A survey in Kerema district in Gulf province found 35% of households had no salt in 2015 [14]. Paradoxically, the National Nutrition Survey found iodine status to be adequate in all four regions of PNG however. This may be because while salt was not available in a large proportion of households on the day of the survey, it was available in these households both before and after the day of the survey, i.e. the whole population is benefiting from salt iodization even though there may be days when

they have no salt, or the population urinary iodine data, which is based on the median urinary iodine concentration from the whole population, is hiding pockets of deficiency in sub-populations with the lowest availability of salt.

The results of this survey, combined with other data on salt availability and iodine status from PNG, suggest a unique situation and an urgent need for a better understanding on salt availability and iodine status of sub-populations in the country if the severe consequences of iodine deficiency on the health of the women and children [1 – 3] are to be avoided. It may be that for the country as a whole, or for certain sub-populations in PNG, salt iodization is not an effective strategy, even when properly implemented, and an alternative or complementary strategy to increase iodine intake is needed. Potential alternative or complementary strategies are fortification of an alternative food vehicle, such as rice or wheat flour, [22] or targeted distribution of iodine supplements to high risk groups) [24]. It is possible however that those communities in which access to salt is low do not have access to another processed food that could be a suitable food vehicle for iodization and the lack of roads may also be a limiting factor to achieving high coverage of iodine supplements.

School children in the 6 – 12 years age group are recommended for the assessment of iodine nutrition in a population because of their easy accessibility in the community and the iodine status is assumed to reflect the iodine status of other members of the community [1]. The school-based approach was used in this study because of the supposedly high enrolments and attendance of both male and female children in primary schools in Karimui-Nomane and Sina Sina Yonggomugl districts [1, 15, 18].

The response rates of 97.3% and 96.6% obtained in Karimui-Nomane and Sina Sina Yonggomugl districts are higher than values reported for similar studies in other districts in PNG [7, 8, 10 – 13].

The median UIC for the children in Karimui-Nomane district (17.5µg/L) indicates insufficient iodine intake and severe iodine deficiency. For the children in Sina Sina Yonggomugl district, the median UIC (57.5µg/L) indicates mild iodine deficiency. Thus, iodine deficiency should be considered as significant public health problem among schoolchildren, age 6 – 12yrs, in both districts at the time of this study. This should be of great concern to program planners in the districts, Simbu province, Highlands region and the National Health Department (NDoH).

The median UIC for children in Sina Sina Yonggomugl was higher than the value reported for schoolchildren in Southern Highlands Province PNG (48.0ug/L) [7], but lower than the

value reported in Honduras (287ug/L), Nicaragua (259ug/L), El Salvador (251ug/L), Chile (565ug/L), Ecuador (590ug/L), Brazil (1013ug/L) and Mexico (1150ug/L) [23].

In Karimui-Nomane the UIC for 77.8% (123/158) of the male and 80.0% (100/125) of the female children was below 50.0µg/L. These values were higher than the 37.0% (51/138) for the male and 45.3% (48/106) for the female children in Sina Sina Yonggomugl district. The median UIC values obtained show that the situation in both districts should be considered critical among the male and female children in the 6 to 12 years age groups at the time of this study. The situation is more critical in Karimui-Nomane district compared to Sina Sina Yonggomugl district.

CONCLUSIONS:

The present study found low coverage of adequately iodized salt and iodine deficiency in school children in two districts of Simbu province, in contrast to the national level data (albeit from 2005) indicating adequate iodization levels of salt in households with salt, and iodine sufficiency at national level. Rather than suggesting a decline in the iodization situation and a subsequent decline in iodine status since 2005, we believe our present study confirms the existence of some communities in PNG which are not easily accessible by road and which, therefore, are at high risk of iodine deficiency, because of low availability of salt. Unfortunately, the risk of iodine deficiency may not be alleviated by improved implementation of salt iodization or education on the importance of iodized salt, because neither of these strategies will address the fundamental problem of salt availability. Rather, it is necessary to ascertain the existence of communities whose access to salt is so constrained as to make salt iodization ineffective, and, if such communities do exist, to identify alternative or complementary strategies in order to increase iodine intake in these communities.

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All the authors declare no conflicts of interest.

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PREVALENCE OF HEPATITIS C VIRUS INFECTION AMONG PATIENTS ADMITTED IN MEDICAL WARDS IN PORT MORESBY GENERAL HOSPITAL

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ABSTRACT:
The major objective of this study was to assess the prevalence of HCV infection among selected patients admitted in the medical wards in Port Moresby General Hospital (PMGH). This hospital based cross-sectional study was carried out in 2012 and 2013. Patients were selected after their routine clinical examination by the clinical consultant during ward round. About 3ml of blood was obtained from the blood already collected for routine laboratory tests. The plasma obtained from each blood sample was stored at – 20 C till required for analysis. The Enzyme-linked Immunosorbent Assay (ELISA) Commercial Kit for qualitative detection of IgM-class antibodies to HCV in human plasma was used for analysis of the plasma samples. Three recommended cut-off points and criteria (Positive, Negative and Borderline) were used for the qualitative interpretation of the results. Appropriate ethical approval and permission were obtained from the various authorities including the Medical Research Advisory Committee (MRAC), National Department of Health (NDOH) PNG. Informed consent was also obtained from the 117 patients selected for this study. The mean age of all the patients was 36.0 ± 13.9 years and their age range was 14 to 63 years. Of the 117 plasma samples 16 (13.7%) were positive for HCV IgM, 11 (9.4%) were borderline and 90 (76.9%7) were negative for HCV IgM. The clinical diagnosis for admission of the 16 patients with positive HCV IgM included 5 (31.3%) with cardiovascular disorders (CVD), 3 (18.7%) with pneumonia, 3 (18.7%) with hepatic liver disease, 2 (12.5%) with HIV and 3 (18.7%) with TB-meningitis. Of the 5 patients with CVD two of them had Rheumatic heart disease with mitral regurgitation. The data obtained in this hospital based study revealed the extent of HCV infection among patients admitted in PMGH with different medical diagnosis. It can be considered as baseline data for healthcare providers to have a first glance at the extent of HCV prevalence among the patients in Port Moresby General Hospital and to a limited extent among the general population in Port Moresby.

Keywords: Hepatitis C Virus, Hospital, Prevalence, Positive, Negative, Borderline, Infection
Submitted October, accepted December 2017

INTRODUCTION:

Hepatitis C virus (HCV) is the major course of both acute and chronic hepatitis, which can range in severity from a mild illness lasting a few weeks to a serious, lifelong illness [1 – 3]. According to the WHO estimates, globally about 71 million people have chronic hepatitis C infection; a

significant number of those who are chronically infected may develop cirrhosis or liver cancer [1]. Although there is no vaccine for HCV currently, antiviral medicines can cure more than 95% of patients with HCV infection, thereby reducing the risk of death from liver cancer and cirrhosis, but access to diagnosis and treatment is low, especially in the resource limited countries [1].

HCV is not only the cause of hepatic manifestations but also causes a significant number of extra-hepatic manifestations (EHMs) [4]. The most common modes of infection with HCV are through exposure to small quantities of infected blood, which may occur through injection drug use, unsafe injection practices, unsafe health care, and transfusion of unscreened blood and blood products [1]. HCV is not spread through breast milk, food, water or by casual contact such as hugging, kissing and sharing food or drinks with an infected person [1].

Diagnosis of liver diseases is routinely carried out in Port Moresby General Hospital (PMGH). Several cases of liver hepatitis and cirrhosis have been reported, however, laboratory investigation of HCV is not a routine procedure in PMGH [5, 6]. The clinical significance of early detection and diagnosis of patients with HCV in PMGH cannot be overemphasized, because the effort to prevent transmission and control HCV requires appropriate information and epidemiological data.

Currently, there are no published data to indicate effective monitoring of HCV prevalence among patients admitted in the clinical wards in PMGH. No published data are available on the prevalence of HCV among patients with liver disease. Thus, the implementation of sensitive and cost-effective programs directed towards enhancing the diagnosis of HCV among patients attending clinics and admitted in ward in PMGH will contribute to a decrease in the prevalence of complications among the severely ill and the vulnerable patients.

The major objective of this study was to assess the prevalence of HCV infection among selected patients admitted in the medical wards in PMGH.

SUBJECTS AND METHODS:

The study site:

The primary sites were the Medical words in Port Moresby General Hospital (PMGH), which is the major, general, specialist and referral hospital in the National Capital District (NCD) and PNG. PMGH is also the Teaching Hospital for the School of Medicine and Health Sciences (SMHS), University of Papua New Guinea (UPNG).

Study Design and Sampling:

This was a hospital based cross-sectional study. All patients admitted to the medical words in PMGH between May and July 2012 and also between April and August 2013 were eligible for enrolment in the study. The patients were selected after their routine clinical examination by the clinical consultant during ward round.

Collection of blood samples and questionnaire data:

The major aim of the study was explained to each of the selected patients and their accompanying relatives before requesting their signed informed consent. About 3ml of whole blood was obtained from the blood already collected for routine laboratory tests requested by the medical consultant. The blood samples were kept in a cool-box and transported to the research laboratory in the Division of Basic Medical Sciences (BMS), School of Medicine and Health Sciences (SMHS) University of Papua New Guinea. The plasma obtained from each blood sample was stored at – 20 C till required for analysis.

A self-designed pretested questionnaire was used to collect demographic data and other information about the patient including the medical cause of admission.

Exclusion criteria:

Patients with normal liver function tests, those that were screened positive for hepatitis A and B, severely ill patients, as determined by the clinical consultant, and those that did not give consent were excluded from the study.

Assay of HCV in plasma:

The Enzyme-linked Immunosorbent Assay (ELISA) Commercial Kit for qualitative detection of IgM-class antibodies to HCV in human plasma (Diagnostic Automation Inc, USA) was used for analysis of the plasma samples. Each plasma sample was assayed in duplicate. This ELISA kit is intended for clinical diagnosis, management and follow-up of patients with HCV infection [Ref]. Internal Bench Quality Control (QC) of the method was carried out according to instructions in the Diagnostic Automation protocol [Ref]. The performance characteristics of the method show specificity of 98.0 ± 2.0%, Sensitivity of 98.48 to 99.22% and Coefficient of Variation (% CV) of 4.5%.

Data analysis and Interpretation:

The statistical package for social sciences (SPSS) version 20 for Windows and Excel MS data pack software were used for statistical analysis of the data. Results were presented as the mean, standard deviation and range for quantitative variables.

In the present study, three recommended cut-off points and criteria were used for the qualitative interpretation of the results [7].

Negative indicates that no IgM-class antibodies to HCV were detected;

Positive indicates that IgM-class antibodies to HCV were detected; this indicates possible acute or chronic infection with HCV;

Borderline indicates that further testing with other analytical system should be conducted [7].

Ethical Clearance:

Approval for this study was obtained from the Ethics and Research Grant Committee in the SMHS, UPNG, and the Medical Research

Advisory Committee (MRAC), National Department of Health (NDOH) PNG. Permission was obtained from the appropriate authorities in PMGH. In addition, signed informed consent was obtained from each subject before using their blood sample.

RESULTS:

Informed consent was obtained from the 117 patients selected for this study. The mean age of all the patients was 36.0 ± 13.9 years; the age range was 14 to 63 years. Of the 117 patients 58.1% (68/117) were male and 41.9% (49/117) were female patients. The mean age of the male patients was 36.4 ± 13.5 years and age range was 14.0 to 63.0 years. For the female patients, the mean age was 35.5 ± 14.7 years and age range was 17.0 to 62.0 years. No statistically significant difference ($p > 0.05$) was obtained between the age of the male and female patients. The mean height of the male patients was 1.64 ± 0.08 meters and the range was 1.45 to 1.80 meters; the mean height and range for the female patients were 1.57 ± 0.08 meters and 1.40 to 1.85 meters respectively.

Of the 117 plasma samples 16 (13.7%) were positive for HCV IgM, 11 (9.4%) were borderline and 90 (76.9%7) were negative for HCV IgM. The mean age of the patients with positive HCV IgM was 39.7 ± 14.0 years and the age range was 14.0 to 63.0 years. For patients with borderline HCV IgM the mean age was 36.2 ± 14.0 years and the age range was 21.0 to 60.0 years.

Gender distribution of the 16 patients with positive HCV IgM showed that 56.3% (9/16) were male patients and 43.7% (7/16) were female patients. Table 1 shows the gender distribution of the patients with positive and negative HCV IgM and on borderline including their anthropometric parameters.

Table 1: General characteristics of the male and female patients with positive and negative HCV IgM and on the borderline

	Positive (n = 16)		**Borderline (n = 11)**		**Negative (n = 90)**	
	Males	**Females**	**Males**	**Females**	**Males**	**Females**
HCV IgM	9	7	7	4	52	38
Mean age± SD (yrs)	34.2±3.7	46.7±11.5	31.4±11.6	45.0±14.7	37.5±13.7	32.2±13.9
Age range (yrs)	14.0 – 63	30.0 – 62.0	21.0 – 55.0	25.0 – 60.0	14.0 – 60.0	17.0 – 62.0
Mean Height (m)	1.64±0.05	1.57±0.06	1.66±0.07	1.58±0.04	1.63±0.08	1.57±0.09
Height range (m)	1.55 – 1.72	1.5 - 1.64	1.56 – 1.75	1.55 – 1.64	1.45 – 1.80	1.4 – 1.85
Mean Weight (kg)	60.8±16.2	52.9±6.4	69.1±17.7	52.8±12.1	58.3±13.1	46.2±8.4
Weight range (kg)	30.0 – 90.0	45.0 – 55.0	50.0 – 100.0	38.0 – 65.0	30.0 – 100.0	32.0 – 64.0
Mean BMI (m/kg2)	22.4±5.7	21.3±1.8	24.9±5.3	21.1±4.3	21.9 ±4.4	18.7±3.1
BMI range (m/kg2)	11.7 – 33.1	18.7 – 24.2	17.3 – 32.7	19.5 – 25.0	11.7 – 32.7	12.5 – 26.0

The clinical diagnosis for admission of the 16 patients with positive HCV IgM included 5 (31.3%) with cardiovascular disorders (CVD), 3 (18.7%) with pneumonia, 3 (18.7%) with hepatic liver disease, 2 (12.5%) with HIV and 3 (18.7%) with TB-meningitis. Of the 5 patients with CVD two of them had Rheumatic heart disease with mitral regurgitation.

DISCUSSION:

Results obtained in the present study indicated that 16 (13.7%) of the 117 plasma samples were positive for HCV IgM and 11 (9.4%) were borderline. According to the WHO expert committee, confirmatory tests should be carried out on the 16 positive samples. The nucleic acid test for HCV ribonucleic acid (RNA) is recommended to confirm if the infection is chronic because about 15–45% of people infected with HCV spontaneously clear the infection by a strong immune response without the need for treatment. Although no longer infected, these patients will still test positive for anti-HCV antibodies [1]. The 11 (9.4%) plasma samples in the borderline group should also be subjected to further testing by either serological method or the nucleic acid test.

The 13.7% prevalence obtained in the present study was higher than the 1.0 to 1.9% prevalence reported for Turkey, Spain and Italy [4]. One of the major differences is that the present study was hospital based study; the sites of the other studies were not indicated by the authors. However, the 13.7% prevalence was higher than the 0.6% (1/154) reported for a hospital based study in Northern Cyprus [4].

Other studies have reported HCV prevalence rates of between 3.2 to 4.1% in countries in North Africa and the Middle East [2, 8]. In Egypt, the prevalence of HCV ranges from 5.0 to 25.0% [8, 9]. In Nigeria, the prevalence of HCV ranges from 4.75 to 30.0% [10, 11].

Although the 13.7% prevalence obtained in the present study was from the screening of patients admitted in the PMGH, nevertheless it can be considered as a baseline study that provides the basis for a more elaborate epidemiological assessment of the prevalence of HCV among the vulnerable groups in PNG.

Such a project will be in line with the policy adopted by the World Health Assembly in May 2016: “Global Health Sector Strategy on Viral Hepatitis, 2016 – 2021” [12]. The strategy highlights the critical role of Universal Health Coverage and the targets of the strategy are aligned with those of the Sustainable Development Goals (SDG). The strategy has a vision of eliminating viral hepatitis as a public health problem and this is encapsulated in the global targets of reducing new viral hepatitis infections by 90% and reducing deaths due to viral hepatitis by 65% by 2030 [12].

It is important for the authorities in PNG to adopt and implement the actions and strategies that

WHO has proposed for the elimination of viral hepatitis as a public health problem. The WHO is working in the following areas to support countries in moving towards achieving the global hepatitis goals under the 2030 SDG Agenda: Raising awareness, promoting partnerships and mobilizing resources, formulating evidence-based policy and data for action, preventing transmission and scaling up screening, care and treatment services [12].

CONCLUSIONS:

The data obtained in this hospital based study revealed the extent of HCV infection among patients admitted in PMGH with different medical diagnosis. It can be considered as baseline data for healthcare providers to have a first glance at the extent of HCV prevalence among the patients in Port Moresby General Hospital and to a limited extent among the general population in Port Moresby. It is hoped that this data provides the basis for a more elaborate epidemiological assessment of the prevalence of HCV among the vulnerable groups in PNG.

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EFFECT OF ETHNICITY ON PAIN PERCEPTION AMONG HEALTHY NIGERIANS

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Running Title: Ethnicity affects pain perception

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ABSTRACTS:
Gender, age and ethnic differences in pain perception have been reported in clinical and experimental research. However, it is not known whether cold and ischemia-induced pain models can explain ethnic-related variability in pain perception. The current study was designed to investigate the effect of ethnicity on pain perception in healthy Nigerians and to assess whether the variability in pain perception is dependent on the circulating level of β-Endorphin. One hundred and sixty healthy volunteers were randomly selected from the four main ethnic groups (Fulani, Hausa, Igbo and Yoruba) in Nigeria. There were 40 volunteers per group. The selected individuals were informed on what they should expect during the study after which their informed consents were requested. Questionnaires were used to obtain the socio-demographic and biodata of each of the consented volunteers. Cold, ischemia and cold+ischemia- induced pains were administered, after which the pain threshold and tolerance were estimated by monitoring the time (seconds) taken for pain to occur and the point at which the subject can no longer withstand the pain. Our results show that Igbo ethnic group has significantly lower threshold in cold-induced pain and significantly higher threshold/tolerance in ischemia-induced pain. No significant difference in pain threshold of all the four ethnic groups during cold+ischemia-induced pain. However, the pain tolerance was significantly higher in Igbo ethnic group when compared with Hausa, Fulani and Yoruba ethnic groups. In addition, the pain tolerance significantly decreased in Hausa and Yoruba compared to Fulani ethnic group, while the pain tolerance was significantly higher in Yoruba ethnic group compared with Hausa ethnic group. Also, the circulating β-Endorphin decreases in all the subjects. The present study demonstrates that ethnicity causes variability in pain perception and this is accompanied with alteration in circulating level of β-Endorphin.

Keywords: β-Endorphin, Pain perception, Threshold, Tolerance, Variability, Volunteers.
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INTRODUCTION:

Pain is the commonest reason why people present themselves in health facilities and responses to pain vary from one person to another. Several factors affect pain perception ranging from psychological to physiological [1]. Ethnicity has been reported to play a role in pain perception as study of Nigerian women in labour showed that Yoruba women have the lowest pain tolerance compared to other ethnic groups [2]. However in situation where acute pain progresses to chronic due to poor pain management, there would be a resultant negative effect on the productivity of the community and in addition an increase in the cost of maintaining the health system [3]. The only way to subdue this burden is to individualize pain treatment and this can be achieved through extensive research on pain perception.

Most knowledge and pharmacology of pain has been obtained from animal studies where communication is a significant limitation to accurate pain evaluation. The assessment of pain in such situation is usually through neurophysiological or behavioural responses in animals [4, 5]. Data obtained from animal studies can only be partially applicable to human because of major differences between species making human experiment on pain perception an imperative study, which can also be an ethical challenge. The main limitation to human experimental pain study is based on chronic studies where comorbidity would affect results [6, 7, 8] but ethically approved studies on healthy consented volunteers would likely remove such limitations. Experimental pain in healthy volunteers is also better than clinical trial because it allows tolerant level for pain stimulus and assessment of corresponding responses which will make study of mechanisms and variations easy to understand [7, 9].

When intensity, duration, frequency and location of pain stimulus in relation to pain response are studied in healthy volunteers, the result can help to individualize pain management which will achieve better results. Modalities like electricity, thermal and mechanical are commonly used to mimic pain in human subjects [10]. However, the present study uses thermal, ischemic and combination of both to investigate the effect of ethnicity on pain perception among healthy Nigerians.

SUBJECTS AND METHODS:

One hundred and sixty (160) healthy volunteers were randomly selected from the four main ethnic groups (Fulani, Hausa, Igbo and Yoruba) in Nigeria. There were 40 volunteers per group. The selected individuals were trained on what they should expect during the study after which their informed consents were requested.

Inclusion criteria for the selection of subjects:

The subjects selected were not diabetic, not hypertensive, had normal sensation (touch, pain, vibration and feeling), not on any medications, not on hospital admission in the last one month, did not have surgery done in the last three month, not suffering from chronic pain syndrome, with no comorbidity and were willing to follow the guidelines, in the protocol, and also voluntarily signing the consent form. The investigation was carried out under approval of the Research and Ethical Review Committee of the University of Ilorin, Ilorin, Nigeria.

Protocol:

The subjects were visited in their home and informed about the study; subsequently volunteers were recruited and administered questionnaires to obtain their biodata and socio-demographic data. Subjects were made to sit comfortably in a reclining chair that provides adequate support for the head, arms and legs. The testing facility was at a comfortable room temperature, and provides a quiet and neutral environment with no distraction. Having informed the subject about the procedures and what to expect during the experiment, the following assessments were performed:

Cold-induced pain:

Cold sensation and pain in humans are mediated by Aδ and C fibres. The subjects were asked to hold a cold gel bag maintained at 00C for as long as possible as described by Fowler et al [11].

Ischaemia-induced pain:

The ischaemic pain testing was based on the method by Plesan et al [12], a blood pressure cuff was placed around the non-dominant arm of the subject. The cuff pressure was inflated to 20mmHg above the subject's systolic pressure. With the pressure maintained, subject performed a hand grip exercise on an elastic ball. The subjects closed their eyes for the entire procedure to minimize distraction and time clues. They were asked to indicate when they first detected the pain and when they could no longer tolerate the pain (to a maximum of 5 minutes). Once pain tolerance was reached, the pressure curve was immediately deflated and end-points were measured in seconds (s) with the process performed 3 times and average of the readings documented [12].

Assessment of pain threshold and tolerance:

The pain threshold is defined as the point between being "about to be painful" and "just became painful" and the time taken for this to occur is recorded in seconds, while the pain tolerance is defined as the point at which the subject can no longer withstand the pain. The time taken for this to occur is recorded in seconds. The processes were performed 3 times and the averages were documented [11, 12].

Biochemical Analysis:

Blood sample was collected into EDTA bottles, centrifuged for 30mins at 3000 rpm. The plasma β-Endorphin was determined using ELIZA kit (Cruz Biotechnology, Canada).

All data were expressed as the Mean ± S. E. M. Statistical analysis was performed using SPSS version 20 software. One-way analysis of variance (ANOVA) was used to compare the mean values of variables among the groups. Duncan Post Hoc test was also used to compare significant difference among groups. A difference between two means was considered to be statistically significant when $p < 0.05$.

RESULTS:

Effect of ethnicity on pain threshold and tolerance during cold-induced pain test: The pain threshold was significantly lower ($p<0.05$) in Igbo ethnic group compared with Hausa, Fulani and Yoruba ethnic groups whereas the pain threshold of these ethnic groups (Hausa, Fulani and Yoruba) did not change significantly ($p<0.05$) when compared with one another. However, there was no significant change in pain tolerance of all the four ethnic groups when compared with one another (Table 1).

Effect of ethnicity on pain threshold and tolerance during ischemia-induced pain test: Igbo ethnic group showed significantly higher ($p<0.05$) pain threshold and tolerance when compared with Hausa, Fulani and Yoruba ethnic groups. However, the pain threshold and tolerance did not change significantly in Hausa, Fulani and Yoruba ethnic group when compared with one another (Table 2).

Effect of ethnicity on pain threshold and tolerance during ischemia+cold-induced pain test

The results showed no significant difference ($p<0.05$) in pain threshold of all the four ethnic groups. However, the pain tolerance was significantly higher ($p<0.05$) in Igbo ethnic group when compared with Hausa, Fulani and Yoruba ethnic groups. In addition, the pain tolerance significantly decreased ($p<0.05$) in Hausa and Yoruba compared to Fulani ethnic group, while the pain tolerance was significantly higher in Yoruba ethnic group compared with Hausa ethnic group (Table 3).

Effect of ethnicity on circulating β-Endorphin during cold, ischemia and ischemia+cold-induced pain: The circulating level of β-Endorphin significantly decreased ($p<0.05$) in all the four ethnic groups during cold, ischemia and ischemia+cold-induced pain respectively when compared with control except for Fulani and Yoruba ethnic groups which did not show significant difference in circulating level of β-Endorphin during ischemia+cold-induced pain test (Table 4).

Table 1: Effect of ethnicity on pain threshold (s) and tolerance (s) during cold-induced pain test

Groups	Fulani	Hausa	Igbo	Yoruba
Threshold	63.31±13.12	53.30±10.08	31.80±0.92^{a,b,c}	37.42±2.01
Tolerance	106.12±12.22	101.01±10.26	86.80±15.55	75.20±12.28

Data are expressed as mean ±S.E.M. n=10. Data were analysed by one-way ANOVA followed by Duncan post hoc test. (a,b,c $p<0.05$ relative to Fulani, Hausa and Yoruba respectively).

Table 2: Effect of ethnicity on pain threshold (s) and tolerance (s) during ischemia-induced pain test

Groups	Fulani	Hausa	Igbo	Yoruba
Threshold	28.40±1.03	30.82±2.00	35.90±1.02^{a,b,c}	23.42±2.20
Tolerance	42.10±5.25	43.81±2.80	76.53±8.50^{a,b,c}	39.90±3.18

Data are expressed as mean±S.E.M. n=10. Data were analysed by one-way ANOVA followed by Duncan post hoc test. (a,b,c $p<0.05$ relative to Fulani, Hausa and Yoruba respectively).

Table 3: Effect of ethnicity on pain threshold(s) and tolerance(s) during cold+ischemia-induced pain test

Groups	Fulani	Hausa	Igbo	Yoruba
Threshold	40.70±5.12	37.40±4.05	39.31±5.00	31.20±3.82
Tolerance	90.10±6.21	56.30±5.18^{a}	160.53±6.30^{a,b,c}	72.60±3.82 ^{a,b}

Data are expressed as mean±S.E.M. n=10. Data were analysed by one-way ANOVA followed by Duncan post hoc test. (a,b,c $p<0.05$ relative to Fulani, Hausa and Yoruba respectively).

Table 4: Effect of ethnicity on circulating level of β-Endorphin (pg/ml)

Groups	Control	CIP	IIP	CIP+IIP
Fulani	48.80±2.22	20.80±4.09*	32.60±2.36*	45.80±5.92
Hausa	54.40±3.21	19.20±5.18*	19.20±3.51*	33.40±2.18*
Igbo	65.60±3.50	15.20±2.44*	24.40±2.06*	38.60±2.77*
Yoruba	82.40±4.82	35.60±1.86*	46.40±6.41*	69.60±4.82

Data are expressed as mean±S.E.M. n=10. Data were analysed by one-way ANOVA followed by Duncan post hoc test. (*$p<0.05$ vs control). CIP; cold-induced pain, IIP; ischemia-induced pain

DISCUSSION:

Considerable evidence has substantially demonstrated ethnic disparities in the prevalence, treatment, progression and outcomes of pain-related conditions [3]. However, there is a dearth in information regarding the mechanism underlying these group differences, although the variability has been associated with variation in quality of sleep [13], vitamin D deficiency [14], socio-cultural factors

that affect coping mechanism [15] and variation in neurological processes among others.

Our current findings show that Igbo ethnic group has the lowest pain threshold during cold-induced pain and the highest pain threshold and tolerance during ischemia-induced pain, while Fulani, Hausa and Yoruba do not show significant difference in pain threshold and tolerance during cold and ischemia-induced pain tests respectively. In addition the study shows no significant difference in pain threshold during cold+ischemia-induced pain across the four ethnic groups. However, the pain tolerance is significantly higher in Igbo ethnic group when compared with Hausa, Fulani and Yoruba ethnic groups during cold+ischemia-induced pain. Also, the pain tolerance significantly decreases in Hausa and Yoruba compared to Fulani ethnic group, while the pain tolerance was significantly higher in Yoruba ethnic group compared with Hausa ethnic group during cold+ischemia-induced pain. Also, the circulating levels of β-Endorphin decreases significantly in all the four ethnic groups when compared with control groups during cold or ischemia-induced pain.

The finding that Igbo ethnic group has the lowest threshold during cold-induced pain seems to be in consonance with earlier study which reported that previous exposure to cold and percentage of body fat affect response to cooling [16]. Igbo ethnic group originated from the Riverine area of Nigeria and they are naturally exposed to cold than other ethnic groups.

In addition, our present study indicates that Igbo ethnic group has the highest pain threshold and tolerance when compared with other ethnic groups during ischemia pain: this suggests variability in pain perception between the Igbo and the other ethnic groups in Nigeria. Also, the significant difference in pain tolerance obtained in the present study during cold+ischemia-induced pain test indicates variability in pain perception among the four ethnic groups in Nigeria. Therefore, the present results show that ischemia-induced pain reflects higher pain threshold and tolerance when compared with cold-induced pain in Igbo ethnic group. This implies that cooling may have significant analgesic properties than ischemic pain: this is in agreement with previous study that cooling of the body reduces pain in patient with fibromyalgia syndrome [17, 18], post episiotomy pain [19], and postpartum perinea pain [20]. Cooling also reduces serum levels of inflammatory markers thereby reducing pain perception [21]. Also, some authors have measured various markers of inflammation in subjects exposed to very low temperatures [21]. Banfi and colleague showed that treating top-level rugby players with whole body cooling (WBC) for 1 week led to reduced rates of pro-inflammatory cytokines (IL-2 and IL-8) and increased levels of anti-inflammatory cytokines (IL-10) [23].

Cooling or cold exposure has been shown to activate components of reticular activating system, such as, locus ceruleus and raphe nuclei, which can result in activation of behaviour and increased capacity of central nervous system (CNS) to recruit motor neurons as well as activating the sympathetic nervous system (SNS) [24]. These increases in blood circulation level of β-endorphin and noradrenalin after a session of cold shower has been attributed to presence of high density of cold receptors in skin which send an overwhelming amount of electrical impulses from peripheral nerve endings to the brain leading to increase production of β-endorphin. This has significant analgesic effect and it does not cause dependence or noticeable side effects [25]. β-endorphin is an endogenous peptide opioid derived from pro-opiomelanocortin, a neurohormone secreted by the anterior pituitary into the systemic circulation.

Endorphins are found in regions of the brain involved in the perception of pain, including the nucleus accumbens and the arcuate nucleus. Although the role of plasma β-endorphin in pain regulation is unclear, plasma β-endorphin levels have been reported to correlate inversely with pain levels in cancer pain [26], chronic daily headache [27] and post- operative pain [25].

These findings indicate that plasma β-endorphin levels are lower in patients with poorly controlled pain, and increase with pain relief. In our present study there was significant difference in plasma β-endorphin of all the four ethnic groups compared to the control groups during cold or ischemia-induced pain test. Our result is in consonance with earlier study that β-endorphin inversely correlates with pain severity [2]. Hence the variability in pain perception in the present study is plasma β-endorphin dependent

CONCLUSION:

The present study demonstrates that ethnicity causes variability in pain perception and this is associated with alteration in circulating level of β-Endorphin.

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CURCUMIN AND PIPERINE: A NOVEL THERAPY IN THE MANAGEMENT OF OSTEOARTHRITIS IN INDIAN PATIENTS

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ABSTRACT:

To evaluate the efficacy and tolerability of fixed dose combination of curcumin and piperine in osteoarthritis (OA), a non-randomized, open labeled, non-comparative, single-centric, and post marketing surveillance (PMS) study was conducted in 166 osteoarthritic patients (73 men and 93 women, mean age: 54.5 ± 12.45 years). Each patient was administered a combination of curcumin 500 mg and piperine 5 mg twice daily for 12 weeks. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used as a tool to assess the efficacy of the fixe dose combination during the 12 weeks therapy. At the end of 12 weeks of therapy, WOMAC score improved significantly ($p<0.0001$) from 65.82 ± 18.10 to 25.12 ± 21.26. Also a significant reduction ($p<0.0001$) was found in scores for pain, stiffness and physical function from 15.03 ± 3.74 to 5.83 ± 4.42, 5.43 ± 1.95 to 1.52 ± 1.56 and 45.57 ± 13.72 to 17.76 ± 16.23 respectively at the end of 12 weeks. Combination of Curcumin and Piperine was effective and safe for the management of osteoarthritis in Indian patients.

Keywords: Curcumin, Piperine, Osteoarthritis, NSAID

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INTRODUCTION:

Osteoarthritis is a common degenerative disorder of the articular cartilage associated with hypertrophic changes in the bone. Risk factors include genetics, gender, past trauma, advancing age, and obesity [1]. The most common symptoms of OA (Osteoarthritis) are pain, stiffness of the joint, crepitation on motion and limitation of joint motion [2].

An imbalance between inflammatory and anti-inflammatory signaling in chondrocytes and synovial cells, with an abnormal activation of cytokine cascades and an overproduction of inflammatory mediators like IL-1β and tumor necrosis factor-alpha which leads to a decrease in collagen synthesis and, by activation of matrix metalloproteinases (MMPs), to a corresponding increase in collagen degradation, with further up-regulation of mediators and effectors like IL-8, IL-

6, prostaglandin E2 (PGE2), inducible nitric oxide synthase (iNOS), and reactive oxygen species (ROS) is the major cause of arthritis [3].

During OA there is a loss of cartilage, the subchondral bone becomes thicker, the subchondral trabecular bone mass decreases and new osteophytes are formed. OA affects the entire joint: the cartilage is damaged, the underlying subchondral bone structure is remodeled, and a chronic inflammation of the synovium develops. The progression of OA involves changes in the production and functioning of various cytokines. The cytokines involved may be inflammatory interleukins (IL-1β, IL-6, IL-15, IL-17, and IL-18) and tumour necrosis factor-alpha (TNF-α) or anti-inflammatory interleukins (IL-4, IL-10, and IL-13) [4].

Current standard of care for patients with OA mainly relies on the use of analgesics and non-steroidal anti-inflammatory drugs (NSAIDs). These treatments have partial efficacy in controlling disease symptoms, and their long-term use has been reported to cause several gastrointestinal, renal and cardiovascular side effects [2].

Traditionally, plants have been used for centuries as a popular method for the treatment of various health disorders [5]. Curcumin is the yellow pigment of turmeric (Curcuma longa L.), the most popular spice in Indian cuisine and a major ingredient of curry powders. Turmeric has a long history of medicinal use, especially to treat inflammation, and many of its traditional uses have been mechanistically validated in cellular systems as well as in animal models of disease. Indeed, with almost 3,000 preclinical investigations, curcumin is one of the best investigated botanical constituents in the biomedical literature [3]. Also, Korea Food and Drug Safety administration has declared turmeric roots as “generally regarded as safe.” Turmeric and curcumin have been found to be safe and tolerable in human clinical trials and systematic reviews [6].

It possesses many beneficial effects including anti-inflammatory, antioxidant, anticancer, antimicrobial, hepatoprotective and anti-hyperlipidemic [7]. Curcumin acts as a master switch of inflammation by acting at the level of pro-inflammatory enzymes (cyclooxygenases (COX) and lipoxygenases) and inflammatory transcription factors (nuclear factor-kappaB (NF-kB) and signal transducer and activator of transcription 3 (STAT3)) and their genomic expression [3].

Curcumin’s potent anti-inflammatory properties have led to active research on its use for a variety of inflammatory conditions, including postoperative inflammation, arthritis, uveitis, inflammatory pseudotumors, dyspepsia, irritable

bowel syndrome, inflammatory bowel disease, pancreatitis, and Helicobacter pylori infection [8]. Curcumin is a potent and established anti-inflammatory dietary botanical component that inhibits all mediators of the inflammatory response such as cytokines, chemokines, adhesion molecules and growth factors, as well as other mediators such as cyclooxygenase-2, inducible nitric oxide, tissue factor and epigenetic alterations [9].

The bioavailability of Curcumin is low due to a relatively low intestinal absorption, and rapid metabolism in the liver, followed by elimination through the gall bladder [7]. Because of curcumin's rapid plasma clearance and conjugation, its therapeutic usefulness has been somewhat limited, leading researchers to investigate the benefits of complexing curcumin with other substances to increase systemic bioavailability [8].

Piperine, a known inhibitor of hepatic and intestinal glucuronidation, was combined with curcumin and administered in healthy human volunteers. Piperine enhanced the serum concentration, extent of absorption and bioavailability of curcumin in humans with no adverse effects. Concomitant administration of piperine 20 mg produced much higher concentrations from 0.25 to 1 h post drug ($P < 0.01$ at 0.25 and 0.5 h; $P < 0.001$ at 1 h) the increase in bioavailability was 2000% [10].

Piperine significantly inhibits the production of two important proinflammatory mediators IL-6 and PGE2. Inhibition of PGE2 production is important due to its central role in triggering pain. Piperine significantly decreased the IL-1β-stimulated gene expression and production of MMP-1, MMP-13 and COX-2 in human OA chondrocytes. MMP13 collagenases play dominant roles in arthritis because they are the rate-limiting components of the collagen degradation process [11].

METHODS AND MATERIALS:

Design and participants:

This was a non-randomized, open labeled, non-comparative, single-centric, and post marketing surveillance (PMS) study to determine the effectiveness and safety of the fixed dose combination of Curcumin 500 mg and Piperine 5 mg twice daily for 12 weeks.

A total of 166 osteoarthritic patients (73 men and 93 women, mean age: 54.5 ± 12.45 years) reporting to Ortho outpatient department (OPD), were screened for the intensity of knee pain on visual analog scale (VAS). Patients complaining of VAS score > 5 were enrolled in the study.

The study was conducted under supervision at SN Jain Hospital, Solapur (Maharashtra, India).

Postgraduate students posted in OPD administered the questionnaire to each patient and data interpretation was done by clinical pharmacologist.

Patient characteristics:

Inclusion and Exclusion criteria: 166 patients with osteoarthritis who gave their informed consent in the vernacular language were included in the study. Eligible patients were in the age range of 21-80 years and were diagnosed to have osteoarthritis assessed as per WOMAC questionnaire (Western Ontario and McMaster Universities Osteoarthritic Index function subscale). This was a post marketing observation study as the combination was already in use for management of osteoarthritis, hence this study did not warrant clearance from the institutional ethics committee.

The exclusion criteria included patients with any of the several conditions listed as follows: concurrent treatment with any non-steroidal anti-inflammatory drug (NSAID), Disease modifying anti-rheumatic drug (DMARD) or any anti-TNF-a therapy or other antiarthritic therapy, treatment with any investigational agent within 4 weeks of screening and intra-articular or parenteral corticosteroids within 4 weeks prior to the screening visit.

Other criteria for exclusion were as follows: Subjects suffering from cardiovascular disease requiring treatment, diabetes, severe metabolic disease, any oncological condition and any planned surgery during the treatment course or undergone surgery prior to 3 months of enrollment. Females who were pregnant or planning to become pregnant and lactating mothers were excluded from the study.

RESULTS:

Evaluation of Signs/Symptoms of Osteoarthritis:

The WOMAC questionnaire was applied to describe and rate the symptoms of OA. The status of OA signs/symptoms was evaluated by the investigator together with the patient at the time of inclusion and at all visits.

Statistical Analysis:

WOMAC score was evaluated using the analysis of variance (One Way ANOVA using Dunnett's multiple comparisons test). Mean WOMAC scores are presented in Tables 1 and 2. Scores for pain dropped significantly ($p<0.0001$) following Conjoint administration from 15.03 ± 3.74 to 5.83 ± 4.42. Also, a significant reduction in pain score was seen at week 8 when compared with baseline from 15.03 ± 3.74 to 8.54 ± 4.35 ($p<0.0001$). The scores for stiffness

in the treatment group were reduced significantly from 5.43 ± 1.95 to 1.52 ± 1.56 ($p<0.0001$) after 12 weeks of treatment. Also, a significant reduction in stiffness score was seen at week 8 when compared with baseline from 5.43 ± 1.95 to 2.7 ± 1.86 ($p<0.0001$). The scores for physical function in the treatment group were significantly reduced, from 45.57 ± 13.72 to 17.76 ± 16.23 during the course of the study ($p<0.0001$). Also, a significant reduction in physical function was seen at week 8 when compared with baseline from 45.57 ± 13.72 to 26.15 ± 14.99 ($p<0.0001$). The mean total WOMAC score reduced significantly ($p<0.0001$) from baseline from 65.82 ± 18.10 to 25.12 ± 21.26 at the end of 12 weeks of therapy as shown in Figure 1. In addition, a significant reduction in WOMAC score was seen at week 8 when compared with baseline from 65.82 ± 18.10 to 37.3 ± 20.14 ($p<0.001$). Comparison of change in WOMAC score between the group and with baseline also yielded significant reductions ($p<0.0001$) in the treatment group. WOMAC score were evaluated using the analysis of variance (One Way ANOVA using Tukey's multiple comparisons test). Change in mean WOMAC scores within the group are presented in Table 3. Tolerability of the fixed dose combination of curcumin and piperine was reported as excellent by the participants to investigators except for 2% patients who reported gastrointestinal side effect, such as heart burn which was of mild intensity and resolved during the course of treatment without discontinuation of therapy.

Table 1 Change of Mean WOMAC Scores after 4, 8 and 12 Weeks of Treatment

	Treatment group			
WOMAC Parameters	**Baseline (Mean ± SD)**	**4 Week (Mean ± SD)**	**8 Week (Mean ± SD)**	**12 Week (Mean ± SD)**
Pain	15.03 ± 3.74	11.95 ± 3.85	8.54 ± 4.35	5.83 ± 4.42
Stiffness	5.43 ± 1.95	4 ± 1.89	2.7 ± 1.86	1.52 ± 1.56
Physical Functions	45.57 ± 13.72	34.6 ± 14.05	26.15 ± 14.99	17.76 ± 16.23
Total	65.82 ± 18.10	50.54 ± 18.45	37.3 ± 20.14	25.12 ± 21.26

Table 2: Change of Mean WOMAC Scores as compared with Baseline

Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Adjusted P Value
BL vs. W4	15.28	10.23 to 20.33	<0.0001
BL vs. W8	28.45	23.4 to 33.5	<0.0001
BL vs. W12	40.7	35.66 to 45.75	<0.0001

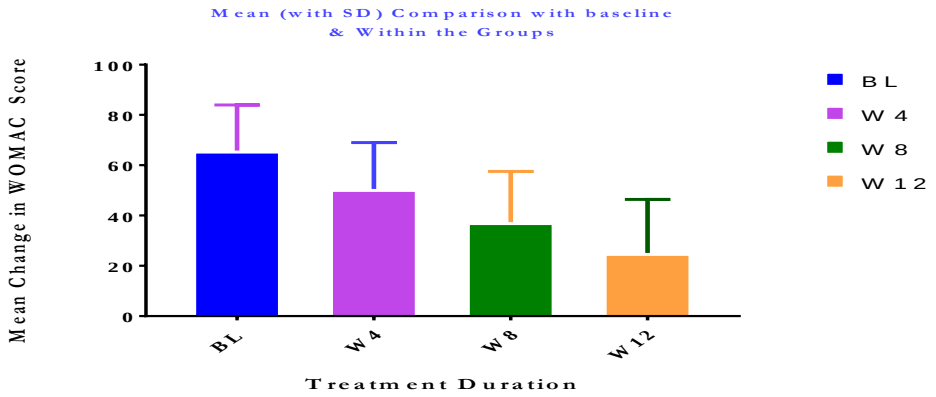

Figure 1: Comparison of WOMAC Score (Mean ± SD) at baseline and follow-up visits

Table 3 Change of Mean WOMAC Scores compared within the group

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Adjusted P Value
W4 vs. W8	13.17	7.652 to 18.7	<0.0001
W4 vs. W12	25.43	19.9 to 30.95	<0.0001
W8 vs. W12	12.25	6.73 to 17.78	<0.0001

DISCUSSION:

Herbal therapies with anti-inflammatory properties and minimum side effects are needed for the treatment of arthritis, including rheumatoid arthritis and osteoarthritis [6]. Pain and osteoarthritis symptoms are known to limit social interactions, and any improvement in these conditions is likely to have a socio-emotional effect. The first evidence for the safety and superiority of curcumin treatment in patients with active rheumatoid arthritis was shown in one pilot clinical study, which evaluated curcumin alone,

diclofenac sodium alone, and their combination, wherein significantly greater improvement was shown by the curcumin group than by the diclofenac sodium group [9]. Nakagawa et al conducted a randomized, double blind, placebo-controlled, prospective clinical study of the efficacy of Theracurmin, a highly bioavailable form of curcumin, in patients with osteoarthritis wherein Theracurmin was significantly effective in decreasing pain and NSAID necessity with no major adverse events [12]. Curcumin has been reported to be effective in alleviating chronic pain in different experimental models, including neuropathic pain, one of the most difficult forms of pain to treat. In an animal model of formalin-induced orofacial pain, curcumin was found to potentiate a subanalgaesic dose (0.2 mg/kg) of diclofenac [9].

In this study significant results were obtained for the efficacy endpoint (WOMAC score) evaluated at week 4, week 8 and week 12. Thus, after 12 weeks of continuous use of Conjoint twice daily, the WOMAC score for OA symptoms decreased by >40%. The significant decrease of all WOMAC items suggests that the clinical improvements observed have a clear mechanistic basis that validates the efficacy of curcumin on joint. Curcumin targets the multiple mechanisms involved in the progression of arthritis and its symptoms. Piperine controls the important inflammatory mediators involved in the pain generation and proteins which degrades cartilage. Also coadministration of piperine enhances the bioavailability of curcumin.

The limitations of the studies were (i) small sample size consisting of 166 subjects, (ii) open label study and (iii) no direct comparison with NSAIDs to determine the effectiveness of Curcumin over existing therapy. However the study provides sufficient evidence to support larger clinical trials that could eventually lead to its acceptance as a standard therapy for many forms of arthritis and possibly other inflammatory conditions.

CONCLUSION:

Osteoarthritis is an age related disorder. The existing therapy has its own limitations of side effects like gastric bleeding or therapy may not be safe in renally compromised patients or at times even the long term therapy may lead to renal impairment. Twelve weeks fixed dose combination of curcumin 500 mg and piperine 5 mg has shown significant reduction in scores for pain, stiffness and physical function. Thus combination of Curcumin and Piperine warrants further investigation as an effective and safe option for the management of osteoarthritis in Indian patients.

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OCCUPATIONAL NOISE INDUCED HEARING LOSS AMONG DENTAL PROFESSIONALS: A REVIEW

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ABSTRACT:
Dental professionals are subjected to noise from dental equipment and instruments throughout the day at work. Although most of the individual instruments have sound emission below the safety level stated by Occupation safety and health administration (OSHA), running of multiple instruments in close proximity for long hours and over several years causes hearing loss in dental professionals. Changes such as irritability, constriction of blood vessels, increase in heart rate and blood pressure, tinnitus and decreased hearing sensitivity is associated with exposure to high levels of noise. Cumulative effect of excess noise can lead to damage to the cochlea causing irreversible damage to hearing. Dentists begin to show reduction in hearing to high frequency sound at 4000 to 6000 Hz but remain unaware of the problem till 28% of hearing loss has occurred. Dental professionals working in a dental school set-up are at an increased risk for noise induced hearing loss due to the proximity to pre-clinical, clinical and laboratory equipment during their work day. Dental students and professionals should be educated about these hazards and advised to use preventive measures to reduce disability. Employees should be informed of the potential for hearing loss and protocols should be in place to make such working environments safer.

Keywords: Occupational hazard, Hearing loss, Tinnitus
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INTRODUCTION:

Sound is a stimulus caused by vibration and detected by the sense of hearing. Noise is an acoustic phenomenon that can occur in gas, solid or at times in liquid. Sound is measured in decibel (dB) for its intensity or by a frequency range (Hertz, Hz) [1]. Sound is audible at the frequency of 20 Hz to 20 KHz [2]. While we are accustomed to the “normal noise” that is present around us, certain professionals are subjected to additional noises in their work environment. Such excess noise can be a potential occupational hazard and care should be taken to minimise disability caused due to such situations.

Noise induced hearing loss (NIHL) is stated as one of the 10 leading causes of work related injuries [3]. The extent of damage to hearing depends on a variety of factors such as the type and intensity of sound, total duration of exposure, duration of individual exposures throughout the day, distance from the source and the age and susceptibility of the individual [3]. Since decibel is a logarithmic unit, an increase by three decibels results in doubling of the sound intensity. While 10 dB of sound is 10 times greater than zero dB, 20 dB is100 times greater than zero dB [1]. This is important while monitoring sound in an environment as well as during efforts of prevention of NIHL.

Properties of noise:

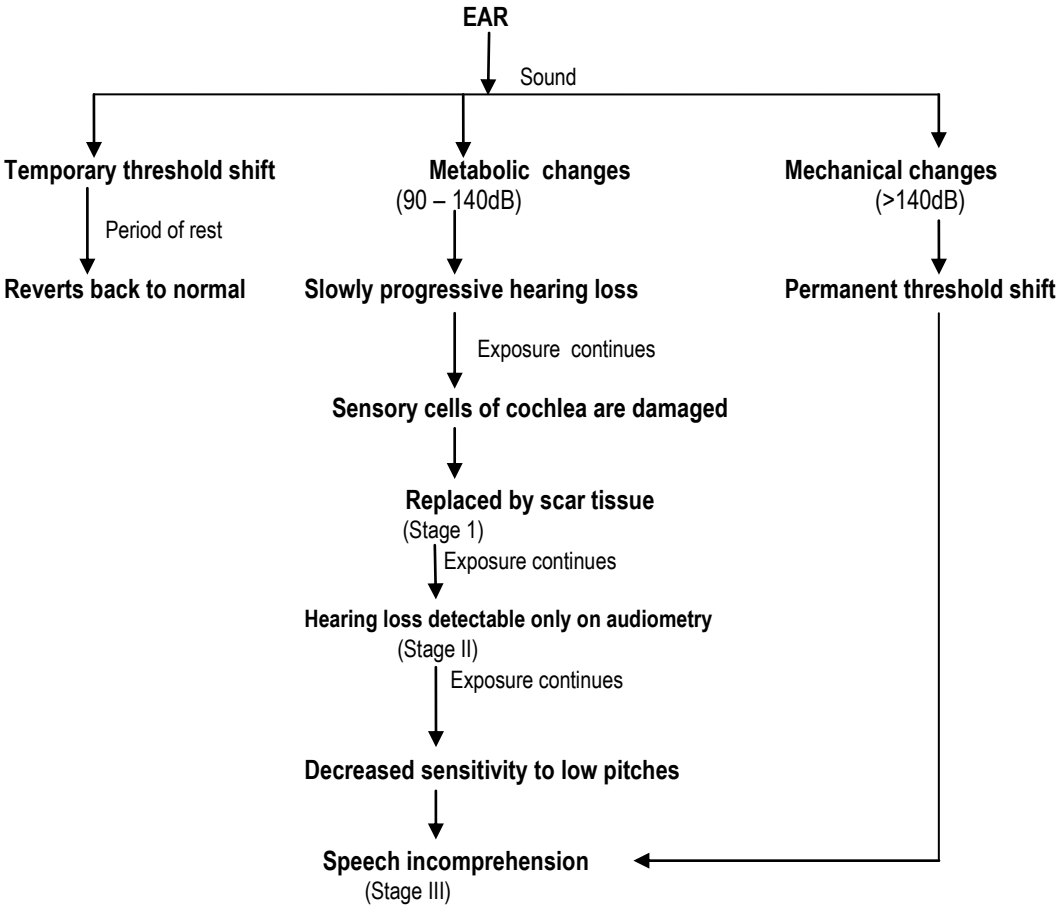
Intensity, duration and spectrum are the three properties of noise that, along with time characteristics and physical make-up determine the risk to hearing [4]. Greater damage to hearing is seen at higher intensity of sound. But this damage is dependent on the temporal patterns of exposure. If the sound is continuous without variations, it is defined as a steady state and if it varies over time, it is defined as fluctuating. Intermittent noise is a combination of hazardous level of noise for certain periods of time with a non-hazardous level of noise. Impulse noise is present only for a short amount of time [5]. According to Feuerstein the greater the duration of exposure to noise, the greater is the damage to hearing. Most of the exposures to noise occur in the complex, variable broadband of signals in the spectrum of sound [4].

Mechanism of loss of hearing:

Changes in the length of the outer cochlear hair induce energy within the cochlea which corresponds to sensitivity to sound intensity and the ability to distinguish between small changes in sound frequency. Damage to this delicate mechanism causes a loss in hearing ability. NIHL maybe temporary or permanent (Figure 1); Temporary loss of hearing is reversible after a period of rest [3]. This is known as temporary threshold shift [4]. Exposure to high intensity noise in the excess of 140 dB even for a short duration causes immediate and permanent loss of hearing known as permanent threshold shift [3, 4]. Here, the delicate tissues of the inner ear are stretched beyond their elastic limits causing a tear. This type of mechanical damage is termed ‘acoustic trauma’ and develops rapidly. Exposure to intensity of sound between 90 and 140 dB induces metabolic changes in the cochlea and causes loss of hearing depending on the duration and level of exposure [3]. This type of hearing loss is slowly progressive over the course of several years and follows three stages. In the first stage, the sensory cells within the cochlea are damaged due to constant exposure to noise. They are later replaced by scar tissue since they do not regenerate. As the exposure continues over a period of weeks or years, the loss in hearing becomes detectable through audiometry. Hearing loss that is detected only through

audiometric tests constitutes the second stage of hearing loss [1]. Pure tone audiometry is the first test that quantitatively detects hearing loss and can be used to assess the nature and degree of damage in adults and children over the age of four years. Otoacoustic emission can also be tested to detect early changes in the inner ear [3]. Use of these tests to detect deficiencies of hearing can help to plan an early intervention and prevent progression of hearing loss. If appropriate testing is not instituted at this stage, it remains undetected by the individual since speech comprehension is not significantly affected [1]. It progresses to the third stage of hearing loss where the patient becomes aware of the loss in sensitivity to sound of lower pitches necessary to understand speech and thus seeks medical attention.[2] Unfortunately, the loss of hearing is permanent at this stage and cannot be improved even with medical intervention.[1] This underlines the importance of monitoring the ambient noise in the environment and taking appropriate steps to prevent loss of hearing before permanent disability has occurred.

Figure 1: Flowchart showing the mechanism of noise induce hearing loss at different sound levels



Effect of noise:

Effect of noise on persons subjected to it can be categorised as non-auditory and auditory. Non-auditory effects include annoyance, irritability, emotional frustration, inability to concentrate, mental fatigue, reduction in work efficiency and productivity, interference with communication and difficulty in speech discrimination.[1,3,6] Auditory effects that are seen include tinnitus, auditory fatigue(90 dB or 400 Hz), temporary deafness (4000-6000 Hz) and permanent deafness (100 dB).[3] Physical effects such as constriction of blood vessels and increase in pulse rate and blood pressure are also seen.[6] Fernandes et al [2] found that noise in a dental classroom environment caused annoyance and negatively affected the metal performance including concentration and visual perception in persons sensitive to low frequency noise in the range of 10-250 Hz. Persons with loss in hearing are also plagued by other problems such as social isolation, inability to effectively communicate with family, co-workers or the public, decreased ability to detect equipment sounds or warning signals in the work environment leading to decreased productivity and increased risk of accidents and increased expenses for procuring hearing aids.[7]

Source of noise in dental office:

Since the advent of ultra-speed air turbine in the 1957 dentists have been concerned about the rise in environmental noise level in the dental operatory. Subsequently a warning was issued in 1959 regarding high turbine machine noises and vibrations.[8] Various equipment and instruments used in the dental office such as electric generators, low speed and high speed angle-design and straight design hand-pieces, autoclaves, laboratory electromotor, compressors, ultrasonic scalers and cleaners, stone mixers, polishers and lathe are sources of significant noise [9]. Myers et al [10] found that low speed hand-pieces produced an average sound pressure of 70.41 dBA (decibel measured using A-weighted scale) while high speed hand-pieces produced a maximum of 83.59 dBA. When suction was used along with the hand-pieces the sound levels increased to 94.77 dBA.[10] According to a study conducted in 1993, slow speed hand-pieces produced sound of 69.71 dB, turbine produced 72.91 dB of sound, laboratory electromotor produced 74.95 dB sound and the highest sound produced was by laboratory machines in the range of 81.42 dB. [11] Klipatrick found that slow speed hand-pieces produced 74 dB, high speed hand-pieces 70-92 dB, stone mixers 84 dB and ultrasonic scalers 86 dB of noise.[12] Fernandes et al [2] in Portugal (60-99 dB) and Kadanakuppeet al [13] in India (64-97 dB) found similar levels of sound in dental school setting.

Risk to dental professionals:

Occupational NIHL is defined as progressive bilateral sensorineural hearing loss that develops gradually over a period of several years because of exposure to continuous or intermittent loud

noise in the work place.[14] In an attempt to decrease the disability caused due to occupational noise exposure, Occupational Safety and Health Administration (OSHA) and National Institute of Occupational Safety and Health (NIOSH) put forward guidelines stating that the maximum permissible exposure limit (PEL) for an eight hour work day was 90 dBA SPL(decibel sound pressure level measured using A-weighted scale). This PEL follows an exchange rate of 5 dB. Therefore, an exposure of 95 dB reduces the permissible working hours to four hours, 100 dB to two hours and so on.[15] Although this PEL is formulated keeping the large scale population in mind, individual susceptibility within this general population can vary greatly.[15] Therefore, care should be taken to avoid exposure to undue noise or to use hearing protection devices (HPD) if avoidance of noise is not possible. Various studies that were conducted to assess the hearing of dentists have been unequivocal in their inference that dentists who have been regularly exposed to noises from dental equipment have reduced hearing while compared with age matched controls. Authors have found that dentists showed abnormal auditory threshold at 4000 and 6000 Hz which is characteristic of NIHL [16,17]. Lazar et al [18] found that dental hygienists who had higher use of ultrasonic scalers reported of difficulty in hearing and tested poorer in pure tone audiometry up to two times more than hygienists who used scalers less frequently. Myers et al[10] found that although none of the instruments used in a dental clinical set up produced sound in excess of the OSHA and NIOSH guidelines and the sound level in dental training operatory was also below the established cut-off level, this could not be compared with a clinical set up where suction would also be used simultaneously thereby increasing the over-all sound level of the environment. Their study subjects reported to the presence of tinnitus and claimed that it got worse at the end of the day [10]. Theodoroff et al [15] found that dental professionals and clinicians who had been practicing dentistry over a period of few years had worse hearing than dental students who were relatively new to the exposure of sound from dental instruments. It was seen that when sound was measured near the operator's ear that was closest to the instrument, the level was sufficiently high enough to cause hearing damage especially with cumulative effect over time.[15]

Bowman et al [19] found that dental students experienced a temporary threshold shift in their hearing after working in the dental laboratories. Singh et al [20] assessed sound levels in a dental teaching institute and found that sound levels were always higher in the laboratories when compared to the levels in clinical set-up even with the suction pump running. They compared the running of multiple air rotors, multiple micromotors and multiple ultrasonic scalers and found that scalers caused higher sound levels than the other instruments [20]. Fernandes et al [2] also found that sound levels in the gypsum and prosthesis laboratory were higher than in

pre-clinical or clinical set-up and that noise was higher for cutting instruments than non-cutting instruments. Parkaret al [6] also found similar results and additionally showed that gypsum lathe trimmers were the noisiest dental instruments and that suction pumps produced more noise when in contact with mucosa than when not in contact. Willershausen et al [8] found that when dentists were compared with other academicians, the former group had higher incidence of impaired air conduction but not bone conduction.

Zubicket al [17] stated that there was a cause and effect relationship between the use of high speed hand-piece and hearing loss since they found in their study that dentists had worse hearing threshold than physicians at the 4000 Hz frequency range and that the right ear of the dentists fared worse than the left due to its closer proximity to working instruments. Right handed dentists show an increased loss of hearing in the left ear and dentists working in a dental school show increased prevalence of hearing defect due to being subjected to the noise of several instruments working at the same time in a medium sized closed room [21]. Although some researches did not find any difference between the hearing ability of dentists and non-dentists or associated the loss of hearing to presbycusis rather than to the noise in dental office, it is still advisable to protect one's ears with HPD when exposed to such potentially harmful noises.[22,23] However, it is seen that dental professionals forgo the use of HPD due to a variety of reasons. While some individuals are unaware or underestimate the danger, others state that they do not use HPD due to discomfort, inconvenience, fear of negative feedback from co-workers and patients or fear of difficulty in communicating with patients [3,15].

Prevention of noise induced hearing loss:

Hearing loss remains undetected until 28% of the damage has occurred.[21] The defect is cumulative, irreversible and potentially detrimental in social and professional situations alike. Dentists show high frequency hearing loss at 4000-6000 Hz in the beginning that slowly progresses depending on the amount and duration of exposure.[20,21]Unlike industrial workers who work in a noisy environment, dental and medical professionals are not bound by any legislature regarding occupational noise levels.[24] Kilpatrick suggested that the distance between a dentist's eye and the working surface should be at least 14 inches or 35 centimetres to prevent excess noise from damaging the operator.[12] An appropriate hearing conservation program that includes noise survey with noise dosimeter and periodic audiometric check-ups, administrative control, engineering control and use of HPD is essential in a dental office.[1,3,21]

Engineering control of acoustics in a clinic should be designed to include wood panels, sound-proof resilient ceilings, carpeting of floors and air conditioners to filter or absorb noise from all sources.[1,21] Compressors and generators

should be stationed outside the operatory. Ambient noise such as office music should be kept to a minimum.[1] Instruments are found to produce higher noise levels as they age and go through more sterilization cycles.[2,18] Hand-pieces should be well maintained and lubricated and old instruments should be replaced with new instruments to decrease the noise produced due to frictional wear.[1,3,20] Simultaneous use of several instruments should be avoided and instruments should be switched on only when required.[1] Contact of suction pumps with the mucosa should be avoided whenever possible.[21]Instruments with added mufflers should be designed to reduce the amount of sound emission [1]. Employees should be informed of the potential for hearing loss and audiometric test should be done at the time of employment and every six years thereafter.[6] Appointment times should be scheduled such that a minimum number of personnel are working with high noise producing instruments at a time. Rotation of employees should be done so that every operator gets placed in a low noise environment to heal the temporary threshold shift. Generic ear plugs made of foam or flanged plastic or custom-made ear plugs called 'musician's ear plug' should be used to protect residual hearing.[20,21] Semi-insert ear plugs in particular can be used since they do not hamper communication between the dentist and the patient and enable the dentist to be aware of surrounding sounds while at the same time being protected from damaging levels of noise.[10] Patients should also be educated about the potential harm to their hearing, however minimal, and offered the use of ear plugs. Patients with hearing aids should be instructed to remove the devices before treatment [21].

CONCLUSION:

It is often seen that dental professionals underestimate their exposure to damaging levels of noise in their work environment. Cumulative effect of acoustic trauma should be taken into account and appropriate measures should be instituted to prevent disability. Employers should ensure that the work place is appropriately planned and that all employees are aware of the associated risks and are provided with adequate measures to protect themselves before irreversible damage is done. Dental curriculum should include education about various occupational hazards and continuing education programs should be directed at methods to reduce noise and protect the hearing of dental professionals.

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CASE REPORT:

DOUBLE JAW SURGERY – A MODIFIED SURGICAL APPROACH TO TREAT SKELETAL CLASS II: A CASE REPORT

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ABSTRACT:
Patients with mandibular deficiency and skeletal class II malocclusions exhibit a wide spectrum of esthetic, cephalometric, and occlusal characteristics. The structure of chin determines facial attractiveness and is directly linked to a quality of life. Correction of dentoalveolar protrusion of maxilla is done by anterior maxillary subapical osteotomy by which anterior segment can be moved superiorly or inferiorly and posteriorly as indicated. Augmentation genioplasty is advocated to improve the overall facial esthetics of patient with mandibular deficiency. In skeletal class II malocclusions cases best results are obtained with double jaw surgery combined with the orthodontic treatment. This is a case report of skeletal class II malocclusion with mandibular deficiency and protruded maxilla in 22 year old female patient who was treated surgically by anterior maxillary subapical osteotomy and augmentation genioplasty along with the orthodontic treatment.

Keywords: Augmentation genioplasty, Double jaw surgery, Orthognathic surgery, Skeletal class II
Submitted April 2017, accepted September 2017

INTRODUCTION:

First jaw deformity correction was performed in the United States of America (USA) by Simon Hullihen, an American general surgeon, in the mid of the 19th century. Surgery is not a substitute for orthodontics but it must be properly coordinated with orthodontics to ensure a better esthetic, functional, and stable results. Class II skeletal deformity is characterized by an exaggerated sagittal distance between the maxilla and the mandible, which could be the result of maxillary prognathism, mandibular retrognathism, or both. Presurgical orthodontic decompensation is essential to enable the surgeon to make a considerable amount of surgical correction, otherwise the esthetic and

functional outcome of the entire procedure will not be satisfactory [1-4].

Case report:

A 22 year old female reported with the complaint of irregular and crowded proclined upper anterior teeth along with retruded chin. Clinical examination of patient revealed a severe skeletal class II. The lateral facial view showed a convex profile, average nose, normal nasolabial angle and retruded chin. Lips were incompetent at rest with lower lip resting behind the upper incisors. Excessive gingival show on smile (Gummy smile) was noted. Intraoral examination reveals class I molar relation. Both upper and lower arches were U shaped. Lower anterior crowding was seen. Excessive overjet was observed as upper anteriors were proclined. Cephalometric analysis revealed increased maxillary vertical height, class II skeletal pattern, and reduced mandible length, proclination of upper and lower incisors. Panoramic view revealed a normal bony trabeculation, the full number of permanent teeth except for extracted impacted upper and lower third molars (Figs. 1a & 1b).

After a complete study and analysis, the detailed treatment plan was explained to the patient. Upper and lower impressions were taken, and study casts were prepared. Mock surgery was performed after knocking out the upper first premolars. Splints were fabricated.

The subapical osteotomy of the anterior maxilla was done after raising full thickness of mucoperiosteal flap and the maxillary components were stabilized using the preformed splint and were fixed with L-shaped 1.5mm titanium plates and screws (Figs. 2a & 2b).

Approximately 4 mm advancement genioplasty was done to correct retrognathic mandible. It was then stabilized with the help of titanium miniplate and screws. Wound was closed with 4-0 vicryl (Figs. 2c & 2d). Splint was kept for 4 weeks. After removal of the splint, occlusion was checked which was found to be stable. Post-surgical orthodontics was carried after 3 months. The profile of the patient improved drastically. The gummy smile had almost disappeared. Lips incompetence was greatly improved.

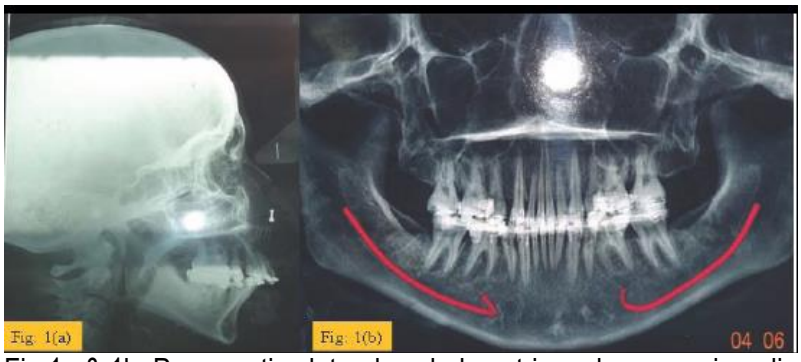

Fig.1a & 1b: Preoperative lateral cephalometric and panoramic radiograph

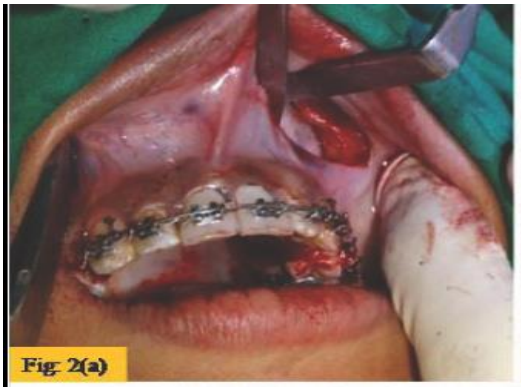

Fig. 2a Subapical osteotomy in upper arch

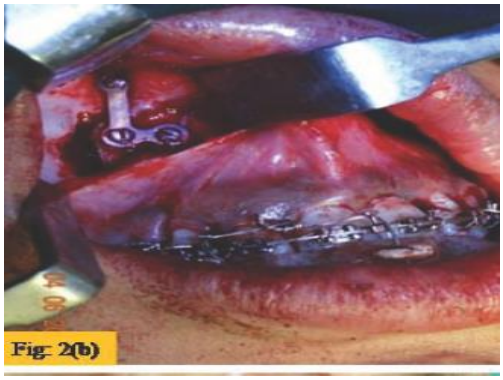

Fig. 2b: Maxillary osteotomy preformed and fixed with titanium plates and screws

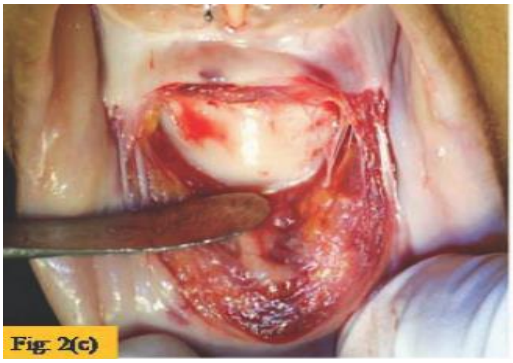

Fig. 2c: Advancement of chin in lower arch

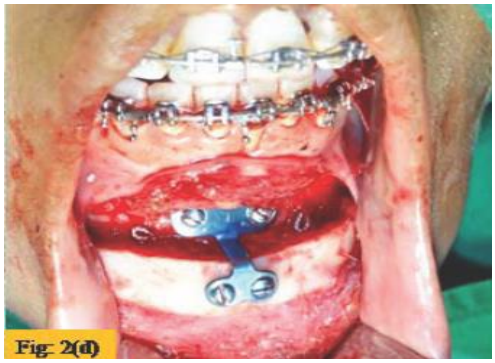

Fig. 2d: Genioplasty was performed and stabilized with titanium miniplate and screws

DISCUSSION:

A class II skeletal malocclusion could be due to maxillary prognathism, mandibular retrognathism, a combination of the two or a vertical growth pattern with a downward and backward rotating mandible and a deficient chin. The envelope of discrepancy deciphers the need for orthodontics, orthodontics with growth modulation or orthodontics combined with orthognathic surgeries [4]. Orthognathic surgery is very important part of the process to correct a dentofacial deformity. The process starts with the initial diagnosis, followed by a treatment plan and patient counselling and consent. Treatment generally begins with a dental assessment and treatment, followed by orthodontic decompensation in preparation for surgical intervention. Orthognathic surgery is followed by postoperative orthodontia to maximize the occlusal relationship [2, 5].

Subapical anterior maxillary osteotomy provides a suitable option in the treatment of maxillary protrusion. It provides improvement of the aesthetic profile without nasal changes [6]. Genioplasty allows 3-dimensional control of chin

position, resulting in significant improvement of facial aesthetics combined with other osteotomies. Of the actual corrections of the chin, advancement genioplasty to improve a receding chin is probably the most common procedure [7-10].

CONCLUSION:

Double jaw surgery with anterior subapical osteotomy and augmentation genioplasty might be recommended as a treatment modality of choice in patients with skeletal class II for best functional and aesthetic results.

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CASE REPORT:

A RARE CASE OF NONSYNDROMIC OLIGODONTIA WITH ANKYLOGLOSSIA

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Running Title: Oligodontia associated with ankyloglossia

ABSTRACT:
Agenesis of teeth and ankyloglossia are common human developmental anomalies. Terms like Oligodontia, Anodontia and Hypodontia are used to describe agenesis of teeth. Oligodontia is a rare condition generally defined as agenesis of six or more teeth excluding the third molars. The condition is not frequently documented in Indian children. There is no much documentation on oligodontia with ankylogossia. Ankyloglossia can adversely affect the development of the surrounding structures including the alveolar process, teeth and can impair functions such as mastication, speech, and swallowing. The present article reports a rare case of non-syndromic oligodontia associated with ankyloglossia in an 8-year old male patient. Oligodontia is a relatively rare condition affecting 0.1-0.2% of the population. Our present case is even rare because of its association with ankyloglossia.

Keywords: Oligodontia, Ankyloglossia, Nonsyndromic, Agenesis.
Submitted in August, accepted in November 2017

INTRODUCTION:

One of the most common developmental anomalies seen in the permanent dentition is the agenesis of one or more teeth [1,2]. It is classified according to the number of missing permanent teeth excluding the third molars [3]. Hypodontia is the congenital agenesis of 5 or fewer permanent teeth; oligodontia is the congenital agenesis of 6 or more permanent teeth, and anodontia is the congenital agenesis of all deciduous and/or permanent teeth [1].

Hypodontia has a prevalence of 1.6% to 9.6% in the permanent dentition, excluding agenesis of the third molars. Oligodontia has a population prevalence of 0.3% in the permanent dentition. Oligodontia occurs more frequently in girls at a

ratio of 3:2 [2,4]. Agenesis of only the third molars has a prevalence of 9% to 37%. In the deciduous dentition, hypodontia occurs less often (0.1%-0.9%) and has no significant sex distribution [2, 4]. The mandibular second premolar is the most common missing tooth following third molar, followed by the maxillary lateral incisor and the maxillary second premolar [2, 5].

The dental agenesis is the result of disturbances in the stages of initiation and proliferation during the formation of teeth. Its etiology is associated with environmental factors such as infections, trauma, chemotherapy, radiotherapy and genetic causes.[1] Oligodontia may also be a part of a genetic syndrome, as a non-syndromic isolated familial trait, as an infrequent finding or as an isolated condition that has been linked to mutations of the MSX1and m PAX9 [6].

The absence of teeth in young patients can cause esthetic, functional and psychological problems particularly if the teeth of the anterior region are involved.[2]

In this paper, we report a rare case of non-syndromic oligodontia with agenesis of ten permanent teeth excluding the third molars in a 8-year old patient along with the presence of ankyloglossia. There appears to be some relationship between ankyloglossia and agenesis of mandibular anteriors.

CASE REPORT:

An 8-year medically fit male patient, accompanied by her parents, reported to the department of Oral Medicine and Radiology with the chief complaint of missing lower front teeth since birth. He had no history of trauma and tooth extractions, without any family history. Further history revealed no teeth ever erupted in this region of the jaw, which suggests that the deciduous incisors were congenitally missing. Extraoral examination revealed, convex facial profile, marked labiomental fold with lip trap and reduced lower facial height. No facial asymmetry was detected. Intraoral clinical examination revealed absence of maxillary lateral incisors and primary maxillary first molars (Figure A) and mandibular central and lateral incisors and the tip of the tongue was attached to the lower alveolar ridge (Figure B). Ankyloglossia which was classified as Class IV by utilizing Kotlow's assessment and was not able to protrude the tongue and his speech was affected. The patient was in the mixed dentition stage. Panoramic radiograph was advised (Figure C). It revealed normal bilateral condyles and coronoid processes with its associated structures. Absence of tooth germs of the permanent teeth in relation to 12, 13, 22, 23, 31, 32, 41, 42, 43, and 44. The remaining permanent teeth were developing normally. Based on the clinical and radiological examinations, the diagnosis of non-

syndromic oligodontia was made. The condition was explained to the parents and patient and treatment plan was discussed. The patient was referred to the department of pedodontics for management of the oligodontia along with surgical intervention for the correction of ankyloglossia.

Fig A: Reveals missing lateral incisors and deciduous first molar

Fig B: Shows congenitally missing lower incisors in association with ankyloglossia

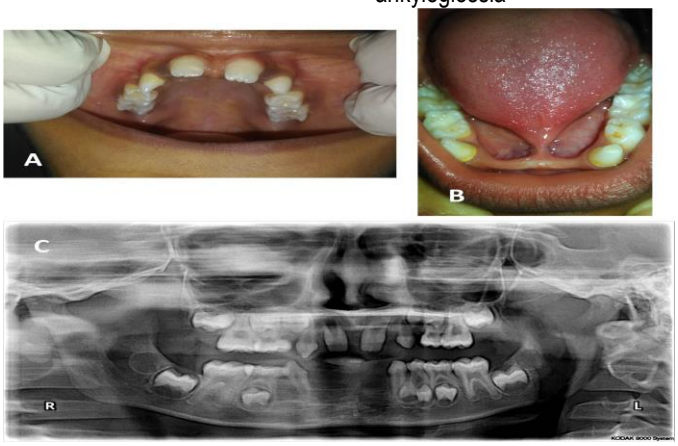

Fig C: OPG shows congenitally missing 12, 13, 22, 23, 31, 32, 41, 42, 43, and 44

DISCUSSION:

Tooth agenesis, the congenital absence of one or more permanent teeth, is a common human anomaly. A tooth is defined to be congenitally missing if it has not erupted in the oral cavity and is not visible in a radiograph [3]. The present case of congenitally missing 10 permanent teeth without any systemic disorders is suggested as isolated or non-syndromic oligodontia. Oligodontia is a rare anomaly, affecting approximately 0.1 to 0.3% of the population [3].

Hypodontia is an anomaly that may result in dental malpositioning, periodontal damage, lack of development of maxillary and mandibular bone height and has significant psychological, aesthetic and functional consequences.[2] The biologic basis for the congenital absence of permanent teeth is partially explained by the failure of the lingual or distal proliferation of the tooth bud cells from the dental lamina.[6]

The etiology of congenital absence of teeth is believed to be rooted in heredity or developmental anomalies.[1,7] Even though

oligodontia is genetic condition, factors such as X-ray therapy, certain medications, infectious diseases, traumas, endocrine and intrauterine disorders, may lead to oligodontia.[1]

Mutation in the transcription factors MSX1 and PAX9 have been identified in families. The factors were demonstrated to be associated with isolated non-syndromic oligodontia.[6] Recent studies have shown that mutation in EDA gene could result in non- syndromic oligodontia.[6] These isolated forms may be sporadic or familial. Familial tooth agenesis can be the result of single dominant gene defect, a recessive or X-linked.[6] Familial relationship suggests that the genes are important but in our present case family history was negative.[3] Oligodontia can occur in association with various genetic syndromes, such as ectodermal dysplasia, Down syndrome, Rieger syndrome , Van der Woude syndrome, Cleft lip palate ectodermal dysplasia syndrome, Oral facial digital syndrome type I, Hemifacial microsomia and others.[2] When oligodontia is associated with a syndrome there may be abnormalities of the skin, nails, eyes, ears and skeleton, which was not seen in the present case.

Oligodontia can be associated with malformations of crown, enamel hypopasia, failure of eruption, microdontia, macrodontia, and germination.[8] In our present case a rare association of oligodontia and ankyloglossia was seen. An extensive search of the current literature indicated that this association has not been reported previously in literature.

Ankyloglossia is defined as “a condition, in which the tip of the tongue cannot be protruded beyond the lower incisor teeth because of short frenulum linguae, often containing scar tissue”. In the present case, fusion of the tip of the tongue was attached to the lower alveolar ridge to the lower lip and missing of the deciduous as well as permanent teeth suggested that there has been a deviation from the normal development in the region of fusion of the first brachial arches. On the review of literature, various classifications of ankyloglossia have been proposed. [9] Thus, our present case was classified as Class IV by utilizing Kotlow's assessment. Frenectomy is the choice of treatment for ankyloglossia.

Panoramic radiography together with clinical examination of the oligodontia is recommended for the detection and confirmation of dental development and performing the diagnosis. [1] Treatment approach has to be case specific and depends on condition of primary predecessor, number of missing teeth, status of occlusion and patient and parent’s preferences. Options include orthodontic therapy, implants, removal partial prosthesis, fixed prosthesis, over dentures and indicated depending on the type of condition. Frenectomy was indicated for ankyloglossia Treatment; it does not only improve speech and

chewing function but also has psychological implications that may greatly help in regaining self-confidence [6].

CONCLUSION:

Complete understanding of rare anomalies like oligodontia and ankyloglossia may be enhanced by reporting of such cases. Such cases should be checked carefully for the presence of any syndromes and should be managed accordingly. Management of such patients generally requires a multidisciplinary approach. Treatment improves speech and chewing function and also has psychological implications that may have a huge impact on self-confidence.

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CASE REPORT:

TEMPORAL, BUCCAL AND MASTICATOR SPACE INFECTIONS IN AN IMMUNOCOMPROMISED PATIENT: REPORT ON A RARE CASE

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ABSTRACT:

"AIDS" is a term used to describe the various clinical syndromes, specific opportunistic infections or malignancies that occur with HIV infection. Oral manifestations are common in people with HIV infection. Oral lesions may be due to decline in immune function. Hence patients with AIDS are subjected to recurrent, life threatening opportunistic infection. Here is a case report of a 70 year old female who presented with right buccal, masticator and submandibular space infection. A routine blood test reveals seropositivity positive for HIV infection. She was treated with antibiotics and underwent an incision and drainage following hospitalization.

Keywords: Masticator, Submandibular space infection, Opportunistic infection

Submitted August, accepted November 2017

INTRODUCTION:

AIDS emerged as a global killer and also increasingly a disease of the poor [1]. Drug users, homosexuals/bisexual contacts, heterosexual contacts, multiple partners, receipt of blood Transmission or blood products, perinatal transmission and in health care settings are the common source for the spread of HIV infections. For the dental practitioner, the significance of intraoral manifestations associated with HIV disease cannot be overstated. Many initial cyclical signs of HIV

infection and AIDS occur in the oral cavity and may serve as markers for early immune deterioration and disease progression [2].

AIDS is associated with several immunological diseases like T-lymphocyte deficiency, B-lymphocyte defects, and macrophage and neutrophil dysfunctions. Individuals with AIDS may have decreased salivary lactoferrin and immunoglobulin A production, which may account for the high incidence of oral infection. With the decline in immune function, individuals with AIDS are subjected to recurrent, life threatening opportunistic infections [3].

Pyogenic orofacial infections usually originate in an odontogenic location [4]. The majority of these odontogenic infections are confined to local lesions, while in some cases they spread from the affected tooth along the anatomic spaces and occasionally advance to a site far from the initial infection. Significant morbidity or even death may occur in the cases that advance into the retropharyngeal, mediastinal, intracranial or intraorbital spaces [5].

This paper highlights a case of an HIV infected female who presented with right Buccal, masticator, and submandibular space infection.

CASE HISTORY:

A 70-year –old female patient presented with a history of pain and swelling in the right side of the face associated with inability to open her mouth since one month. The swelling gradually increased over time and the patient had sought treatment from a district clinic and was prescribed a week's course of antibiotics.

On examination, there was a large diffuse swelling over the right, extending from midline of the scalp to inferiorly till submandibular region. It was soft and tender to touch with local rise of temperature and fluctuation present (Figure1). Intraoral examination reveals marked trismus with mouth opening about a half finger-breadth. Generalised mobility of teeth present due to severe periodontal infection. Grade III Mobility seen in lower right molars with vestibular obliteration and tenderness present.

Extrinsic stains present over the teeth surface due to excessive tobacco chewing habit along with severe halitosis due to poor oral hygiene (Figure 2). Bilateral Submandibular and cervical lymph nodes were mobile, tender on palpation. Patient was advised to get routine blood examination. Routine Blood report revealed that patient is positive for HIV infection.

Patient was referred for surgical management. Patient did not turn up for the further follow up treatment procedures.

Fig. 1: Showing Right Temporal space infection

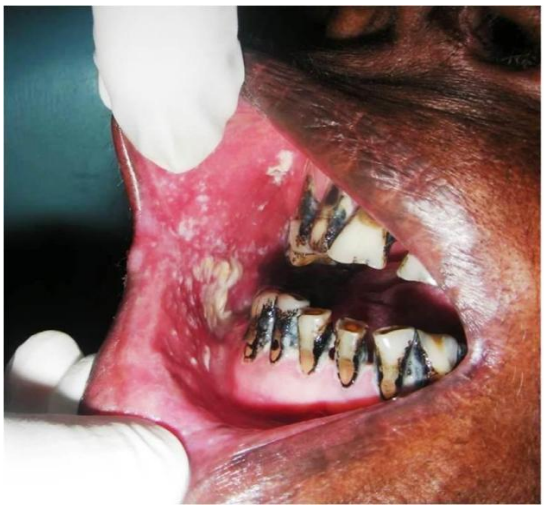

Fig 2: Restricted mouth opening due to involvement of Masticatory space

DISCUSSION:

AIDS patients are subject to a variety of opportunistic bacterial infections in the oral cavity. *P. gingivalis, P. intermedia, F. nucleatum, A. actinomycetemcomitans, W. recta, E. corrodens, P. micros, Capnocytophaga spp.* are the commonly found bacterial species in HIV infection [6].

Infections from the body of the mandible pass more through the relatively thinner lingual plate into the medial spaces while that from the body of the maxilla pass more via the relative thinner buccal plate into the lateral spaces. In addition, the ramus of the mandible serves as attachment on the outer side for masseter muscle which separates the submasseteric and supramasseteric spaces and on the inner aspect; there is attachment of medial pterygoid muscle which separates the pterygomandibular and lateral pharyngeal spaces. Infections can track upwards into the infratemporal fossa between the attachments of the lateral pterygoid and temporalis muscle and into the supratemporal fossa leading to scalp abscess [7].

The masticator space is a distinct deep facial space, bounded by the superficial layer of the deep cervical fascia. It contains the ramus and posterior body of the mandible, and the four muscles of mastication, including the medial, lateral pterygoid muscle, temporal muscle and masseter muscle. It is commonly known that the contracture of medial and lateral pterygoid muscle in response to inflammation causes trismus and pain of Temporomandibular Joint [8].

The temporal space is posterior and superior to the masseteric and pterygomandibular spaces. Bounded laterally by the temporalis fascia and medially by the skull, it is divided into two portions by the temporalis muscle. Swelling is

evident over the temporal area, posterior from the lateral aspect of the lateral orbital rim. Trismus is always a feature of this infection, caused by involvement of the temporalis muscle [3]. The buccal space contains the buccal pad of fat, Stenson's duct and facial artery.

Clinically marked cheek swelling occurs. Submandibular space infection are commonly seen because of odontogenic infections by the second and third molar teeth as their root apices lie inferior to the mylohyoid line of muscle attachment [3].

Oral disease occurs disproportionately among individuals from low socioeconomic levels and among those who are most vulnerable because of poor general health. This is associated with lack of access to care and lower education levels. Improving oral health within these communities will require changes at a number of levels [9]. Oral health is integral to general health.
Oral manifestations are common in people with HIV infection due to decline in immune function [10, 11].

For dental practitioners, the medical evaluation of patients with HIV is three-tiered. They are: Complications that may arise during dental therapy secondary to a patient's immunologic, haemostasis and pharmacotherapeutic status; Medical conditions that may directly interfere with provision of dental procedures; Patient's prognosis for survival;

Dental providers need to continue to render dental care to all patients, regardless of their social or religious background or sexual orientation. The provision of dental care for HIV infected individuals is similar to that of non-infectious patients.

The basic principles in treating any space infection are antibiotic therapy, removal of the source of infection and incision and drainage of the infected space and airway maintenance among other forms of supportive care [2].

CONCLUSION:

Controlling a focal infection within the oral cavity may eliminate adverse consequences such as systemic infections. Early and aggressive management can prevent major complications.

ACKNOWLEDGEMENT:

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CASE REPORT:

FANCONI'S ANEMIA: A CASE REPORT

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ABSTRACT:

Fanconi's Anemia (FA) is a rare autosomal recessive disorder characterized by thrombocytopenia,diverse congenital malformations which include skeletal malformations, hyperpigmentation, urogenital, renal and cardiac anomalies. We report a case of Fanconi anemia who presented with thrombocytopenia, bilateral hypoplastic thumbs, café-au-lait spots, with severe bleeding from the gingiva managed with platelet transfusion and extraction of the tooth was done

Keywords: Fanconi's anemia (FA), Thrombocytopenia, cafe-au-lait spots, squamous cell carcinoma.
Submitted November, Accepted December

INTRODUCTION:

Fanconi Anemia (FA) is a rare autosomal recessive disorder (birth incidence of 1 per 350000), first described in 1927 as progressive lethal anaemia associated with brown pigmentation of skin [1, 2]. The disorder includes pancytopenia with hypoplastic bone marrow, skeletal, renal and ophtalmological malformations and chromosomal aberrations [3]. It also involves many organs including skin and genitourinary, musculoskeletal, neurological and cardiovascular systems. The clinical findings in FA patients are Hyperpigmentation on the skin, small reproductive organs in males, kidney problems, abnormalities in the thumbs and arm, skeletal anomalies of hip, spine or ribs, low birth weight, short stature, growth retardation, defects of the tissue separating the heart chambers and mental retardation or learning disability [3, 4]. Most cases of FA manifest anemia symptoms during childhood. However, the symptoms may not become apparent until adulthood [5, 6]. FA patients are at risk for developing secondary malignancies, for example leukaemia, squamous cell carcinoma and hepatocellular carcinoma [7-9]. The risk of squamous cell carcinoma development is high in the anogenital region as well as the head and neck region [10]. There is increased susceptibility of the oral cavity and

anogenital region to local predisposing factors like environmental toxins and viruses [5].

CASE REPORT:

A six year old boy reported to the department of oral medicine and radiology Yenepoya Dental College with the chief complaint of bleeding from the gums since 2 weeks. History revealed similar bleeding from the gums frequently, family history revealed his elder brother with the same problem and died at the age of 3 years. On general physical examination he was conscious, cooperative, poorly built, vital signs were within normal limits. Patient had microcephaly, triangular facies, bilateral anopthalmos, hypertelorism, depressed nasal bridge. High arched palate, low set ears, webbed neck, widely spaced nipples, bilateral undescended testis, radially curved left forearm and hypoplastic biphalangial thumb attached to the palm by thin thread like pedicle. Café au lait spots were noted on the right side of the skin over the neck and shoulder.

Intra oral examination revealed gingiva which was erythematous, soft and edematous. Grade 3 bleeding on probing, chronic pulpitis in relation to 16, 26, 75, 85 and 46. (Figure 1)

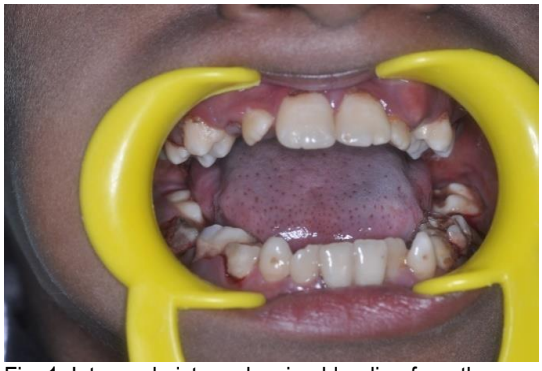

Fig. 1: Intra oral picture showing bleeding from the gingiva, chronic pulpitis 75

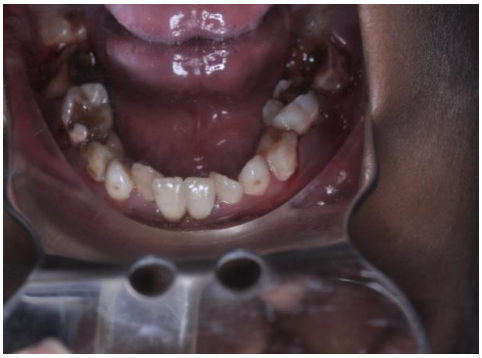

Fig. 2: Postoperative picture after extraction of 75

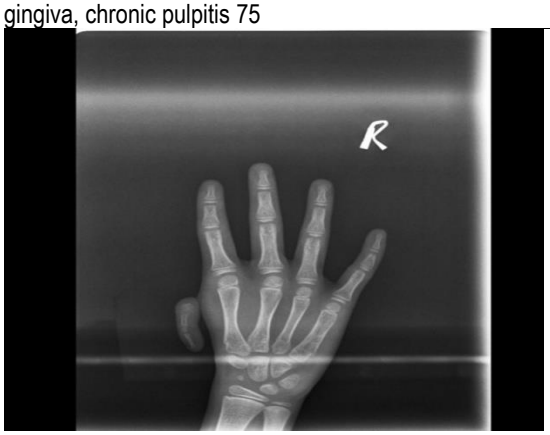

Fig. 3: Right hand wrist radiograph showing hypoplastic thumb, rudimentary 5th Meta carpel bond

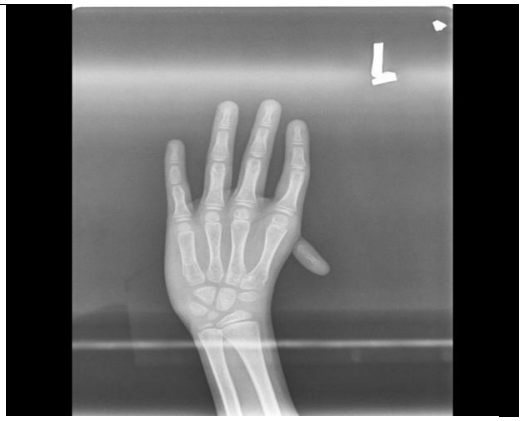

Fig. 4: Left hand wrist radiograph showing hypoplastic thumb

Based on the chief complaint, history given by the parents and clinical evaluation, it was provisionally diagnosed as fanconis anemia, chronic generalized gingivitis and chronic pulpitis 16, 26, 74, 75, 85 and 46 were made.

Hand wrist radiograph revealed hypoplastic thumb, rudimentary 5th Meta carpel on right side (Figure 3). Panaromic radiograph revealed normal anatomical land marks, coronal radiolucency involving enamel dentin and pulp in relation to 16, 26, 74, 75, 85 and 46.

Electro cardiograph showed dilated cardiomyopathy. Hematological investigations show platelet count was 5000/ml, blood slide of peripheral smear showed normochromic blood picture with thrombocytopenia, RBC count was 4.25 million /cu mm, Hb was 12.6/dl, PCV was 34.6%. Based on the radiographic finding and laboratory finding Fanconi anemia was confirmed.

Patient was hospitalized immediately and 4 units of platelet transfusion were given. Post transfusion platelet count was 63000/ml. The next day 2 units of platelet transfusion was done prior to extraction of 75 under local anesthesia with prophylactic antibiotics coverage and 1 unit of platelet transfusion were done immediately after teeth extraction. Patient was fine and there was no report of bleeding. Patient was discharged from the hospital after 2 days.

DISCUSSION:

Fanconi Anemia (FA) is a rare autosomal recessive syndrome. The disease is named after the Swiss paediatrician Guido Fanconi who originally described the disorder in three brothers, in 1927 [1]. Fanconi anemia is remarkable; its phenotype heterogeneity includes bone marrow failure and a variety of congenital malformations. Fanconi anemia has been found in a variety of ethnic groups.

Our present case had growth failure, skeletal malformations, café- au- lait spots, bone marrow failure and absence of left kidney. The hematological disorders resulting from bone marrow dysfunction (thrombocytopenia, leucopenia and anemia) usually appear around a mean age of 7 years, but they can arise very early at birth or even more rarely around 40 years of age [3].

Our case has thrombocytopenia at the age of 5 years. Some patients with FA are prone to develop different types of cancers, commonly leukemia acute myloid leukemia (AML), less commonly liver tumors, cancers of mouth, tongue, throat, genitals and brain tumors. Classic phenotype of FA includes, short stature, abnormality of the thumbs, microcephaly, café au lait and hypopigmented spots with characteristic facial appearance (a broad nasal base, epicanthal folds, and micrognathia) [2]. Our case presented with all these findings. FA newborns commonly have hypogonadism and renal malformations [2,3]. Radial ray abnormality is the most common physical abnormality noted in patients with FA during infancy. Bilateral radial

ray defect is more common (78%) than unilateral (22%) [3]. Hematologic abnormality at birth is very rare [4].

Differential diagnosis considered in the present case includes thrombocytopenia-absent radius (TAR) syndrome, VATER /VACTERAL syndrome and Holt- oram syndrome. TAR syndrome presents at birth with severe thrombocytopenia with bleeding manifestations and radial ray defects [5]. Microcephaly, short webbed neck and skeletal anomalies noted in the present case, though rare, have been reported in patients with TAR syndrome [2,3]. In FA, if the radii are affected, the thumbs are always abnormal (absent /hypoplastic); in TAR radii are absent but the thumbs are always present [2]. The present case had an abnormal thumb, consistent with the diagnosis of Fanconi anemia.

FA has considerable overlap in the physical abnormalities with VATER /VACTERAL syndromes. In a large series of FA patients, 10% patients had three principal clinical features and additional 20% patients had two major defects found in VATER syndrome [6]. Therefore, FA patient can be easily misdiagnosed as VATER/VACTERAL syndrome. The present case had vertebral and limb defects. VATER or VACTERAL syndromes are sporadic whereas FA has 25% chance of recurrence and misdiagnosis has severe consequences for genetic counseling [7]. Therefore it is recommended to rule out FA in patients with suspected VATER / VACTERAL syndromes by chromosomal testing [3,6]. Holt-Oram syndrome has radial ray defects with cardiac defects (100% cases). In the present case there were no cardiac defects [5]. Trisomy 18 can rarely have radial ray defects and eye anomalies. However trisomy 18 has host of different physical abnormalities and a typical facies [2]. Diagnosis of FA requires high index of suspicion as it presents with physical abnormalities involving multiple systems and hematologic abnormalities at birth are extremely rare. Early diagnosis in FA is very important as long term survival depends on the age of onset of hematologic abnormalities or malignancies [8].

If FA is recognize in the preanemic phase, drugs and environmental insults implicated in acquired aplastic anemia or malignancy can be avoided and life span can be prolonged [2]. Early diagnosis also offers options of planning next pregnancy; as the umbilical cord blood can be used for stem cell transplantation. Bone marrow or umbilical cord blood transplantation from identical sibling is now considered the treatment of choice for FA. [3,7]

CONCLUSION:

Fancooni FA patients develop thrombocytopenia at childhood it is recommended to check for thrombocytopenia, requires platelet transfusion for extraction of the tooth. Regular follow up is recommended to screen the developing malignancies. Early diagnosis also offers options of planning next pregnancy as the umbilical cord blood can be used for stem cell transplantation.

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