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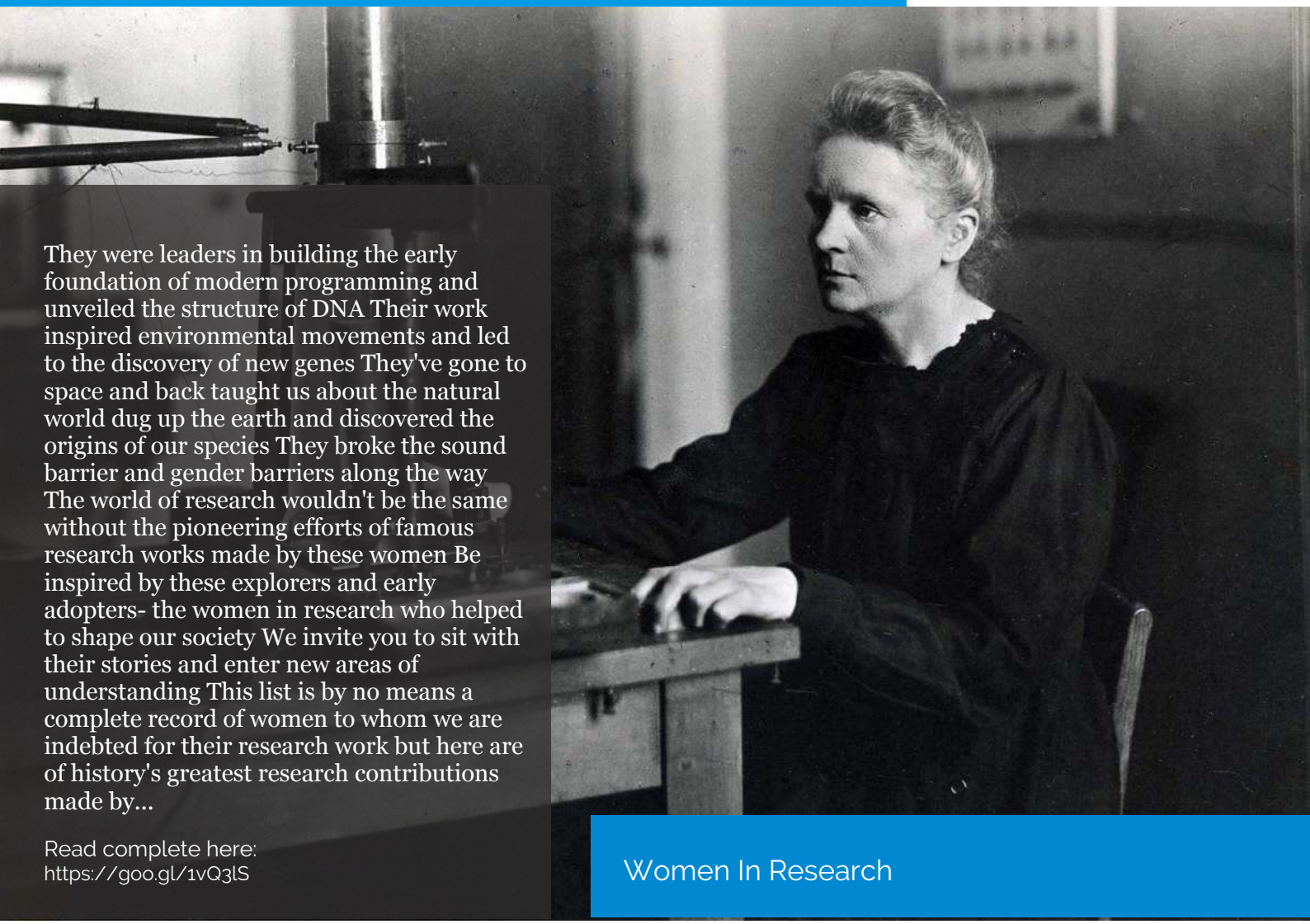

They were leaders in building the early foundation of modern programming and unveiled the structure of DNA Their work inspired environmental movements and led to the discovery of new genes They've gone to space and back taught us about the natural world dug up the earth and discovered the origins of our species They broke the sound barrier and gender barriers along the way The world of research wouldn't be the same without the pioneering efforts of famous research works made by these women Be inspired by these explorers and early adopters- the women in research who helped to shape our society We invite you to sit with their stories and enter new areas of understanding This list is by no means a complete record of women to whom we are indebted for their research work but here are of history's greatest research contributions made by...

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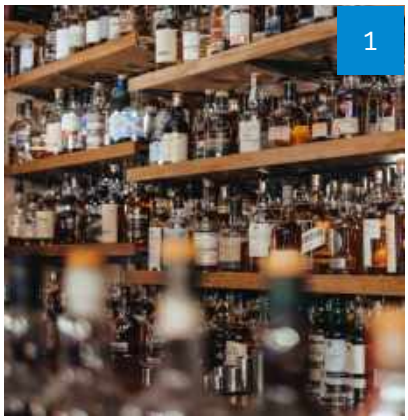

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Adoption of Institutionalized Children and the Additional Risks of Fetal Alcohol Spectrum Disorder (FASD); A Review for Clinicians, Adoption Staff and Parents

Gideon Koren & Asher Ornoy

Ariel University and Motherisk Israel

ABSTRACT

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The objective of the present review is to estimate the risks of abnormal development among institutionalized children, addressing either the risk in general, or the risk for fetal alcohol spectrum disorder (FASD).

Methods: We conducted a narrative review for studies measuring developmental effects of these populations. We identified all systematic reviews and meta analyses dealing with either the associa- tions between institutionalization of children and their neurodevelopment in general, or their likelihood of suffering from FASD.

Results: In a meta-analysis the mean IQ/DQ was 84 among institutionalized children, as compared to 104 among children raised in families. Favorable caregiver-child ratios had a protective effect, whereas longer stays in institutions had a detrimental effect on IQ/DQ. One or more years of family life prior to institutionalization provided a partial protective effect.

A further meta- analysis has shown a positive impact of adoption on children's cognitive development with adopted children displaying remarkably normal cognitive competence as compared to their non-adopted peers.

Keywords: institutionalization, fetal alcohol spec- trum disorder, FASD, malnutrition, neglect, adoption, foster homes, children's home.

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A further meta- analysis has shown a positive impact of adoption on children's cognitive development with adopted children displaying remarkably normal cognitive competence as compared to their non-adopted peers.

In a meta- analysis , the overall pooled prevalence of FASD was 6% for full blown fetal alcohol syndrome (FAS), and 16.9% for the whole range of FASD. The estimated prevalence of FASD was 10-40 fold higher than in the general population.

Conclusions: A large proportion of adopted institutionalized children may not follow a normal developmental trajectory. The risk for FASD is 10-40 higher than in the general population and the institutional environment negatively affects the child's development.

Keywords: institutionalization, fetal alcohol spectrum disorder, FASD, malnutrition, neglect, adoption, foster homes, children's home.

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I. INTRODUCTION

Between 1999-2014 about a quarter of a million children were adopted in the United States with the origin of the adopted children from China (74,000), Russia (46,000), Guatemala (30,000) and South Korea (20,000) leading in numbers[1].

Many of these children, and especially from the former Soviet Union, had been institutionalized at the time of adoption. There is ample evidence that institutional care is associated with "structural neglect" characterized by suboptimal physical resources, minimal staffing, extreme neglect and lack of adequate caregiver-child interactions[2] .

Consistent evidence suggests that these may adversely affect the physical, hormonal, cognitive, behavioral and emotional wellbeing of many of these children. While there is still a debate whether there is a distinctive "post-institutional syndrome", many of these youngsters sustain neuro-behavioral and emotional impairments[2].

Summarized by Bledsow and Johnston[3] , the chances of a child to follow a normal trajectory at the time of adoption are limited. Destitute, single mothers with poor prenatal care and inadequate diet , are common causes for children to be given for adoption.

In addition to the multifaceted insult caused to the child by being institutionalized, a large percentage of the single mothers that drop these children in the typical "children's homes" consume alcohol and drugs of abuse, rendering the fetus vulnerable to the detrimental effects of illicit drugs, especially fetal alcohol spectrum disorder (FASD)[3] .

Recognizing FASD is therefore critical in any attempt to evaluate medically adopted children from "children's homes".

II. FETAL ALCOHOL SPECTRUM DISORDER (FASD)

Fetal Alcohol Spectrum Disorder (FASD) describes a range of adverse physical, behavioural and cognitive effects following ethyl alcohol (herein named alcohol) exposure during embryonic and fetal life. The 'spectrum' term allows a wide range of severity of neurodevelopmental effects[4] . The full blown syndrome is characterized by a triad of pathognomonic features that include; distinctive craniofacial dysmorphology (reduced palpebral fissure length, smooth filtrum, thin upper lip), intrauterine growth restriction (IUGR), and central nervous system (CNS) developmental abnormalities[4-5] . Identification of alcohol abuse during pregnancy is heavily stigmatized with rare prenatal screening attention in routine care[6] .

Presently, the lower limit of safety of maternal alcohol consumption during pregnancy on fetal development has not been determined , and virtually all medical organizations call for abstaining from any alcohol consumption during pregnancy [7] . Binge consumption has been associated with FASD risk, and second and third trimester alcohol consumption increases FASD risk five-fold over first trimester consumption[8] .

Individuals with more subtle impairments tend to have poorer quality of life outcomes due to lack of recognition of their neurological deficits[9] . Secondary disabilities associated with FASD, such as dependent living, incarceration, early death, addictions, and early school drop-out, may be preventable with early diagnosis and medical/social/educational interventions[9-11] . It is critical to note that not all chronically exposed infants will exhibit alcohol-related neurotoxicity. Rather, an estimated 40% of chronically exposed fetuses will exhibit diagnosable FASD[12].

The majority of children with FASD display attention-deficit hyperactivity disorder (ADHD), oppositional defiance disorder, depression, and conduct disorder[13-15] . Lack of widespread recognition of FASD by medical, law enforcement and judicial authorities has led to very large numbers of affected individuals experiencing substantial difficulties without consideration of their cognitive and behavioral limitations[16] .

III. FETAL EFFECTS OF ILLICIT DRUGS

While most illicit drugs (opiates, cocaine, amphetamines, cannabis, hallucinogens) do not appear to increase the rate of congenital malformations or induce a specific syndrome, they certainly have significant neurobehavioral effects [17-20]. Moreover, many of these addicted women are polydrug users [17, 18]. Drug abuse, especially alcohol abuse during pregnancy, is more prevalent among mothers of institutionalized children[21] . Thus, institutionalized children suffer not only from neglect and emotional deprivation, but often also from the consequences of prenatal exposure to illicit drugs.

Heroin abuse during pregnancy is linked to delayed early developmental milestones especially if the exposed children are raised in their biological homes[17-19] . This is in addition to increased rate of prematurity, intrauterine growth restriction and increased complications of pregnancy. At school age they exhibit increased rate of learning difficulties especially in mathematics and reading and a very high rate of attention deficit hyperactivity disorder (ADHD) [20] .Interestingly, it was found that a major cause for these neurobehavioral changes is the negative home environment, as children born to heroin dependent mothers who were adopted at a very young age exhibit normal early developmental milestones [19-20]. However, early adoption reduces only slightly the rates of ADHD.

Prenatal cocaine exposure is associated with a high rate of prematurity, fetal growth restriction and slightly reduced head circumference at birth [17-18]. While there seem to be no motor deficits, there is a significant increase in the rate of "soft neurological signs" manifested at preschool and school age by high abnormal scores on the externalizing and internalizing behavioral indices of the Child Behavior Checklist (CBCL), generally implying a higher rate of ADHD and learning difficulties. Of interest, these neurobehavioral changes were more common following prenatal exposure to both cocaine and heroin. The highest neurobehavioral abnormalities were found following prenatal exposure to cocaine and alcohol[17].

Prenatal exposure to methamphetamine was also not associated with an increased rate of congenital malformations. However, there were distinct neurobehavioral problems[22-23]. In the IDEAL study, children born to methamphetamine-dependent mothers were followed from birth to 7.5 years of age[23] . At the age of 3 years they exhibited a high rate of behavioral and attentional problems, at 5 years there was also some increase in anxiety/depression, externalizing, and attentional problems. At early school age (about 7.5 years) there was a higher rate of ADHD, a higher rate of externalizing problems on the CBCL and a high rate of misconduct and aggression. Any additional abuse of alcohol combined with the above described illicit drugs further increased the neurobehavioral damage[17-18] .

IV. OBJECTIVE

The objective of the present review is to define the developmental trajectory among institutionalized children, addressing either the risk in general, or the risk for FASD.

V. METHODS

We conducted a narrative review of PubMed, Embase and Cochrane databases from inception to April 15, 2019 for all human studies reporting a systematic review and meta- analysis on child development among institutionalized children. We included any systematic review and meta analysis that reported on neurodevelopment of institutionalized children using the terms "institutionalized children"/"children's home"/ "abandoned children"/ "child development"/ "cognition"/ "IQ"/ FASD/ alcohol in pregnancy/ AND "systematic review" and "meta analysis". The analysis looked at either neurodevelopment in general, and also for studies where the assessment was focused on FASD.

Because in both cases of risk estimates (i.e. in general and specifically for FASD) comprehensive meta- analyses have been published, we did not attempt to reproduce them, but rather to apply some of their statistics for calculating overall risks.

VI. RESULTS

Out of 5,872 articles dealing with FASD or instititutionalized children, we identified 4 systematic reviews and meta analyses addressing the two issues aimed: development of institutionalized children[24,26], and FASD among institutionalized children[27-28].

6.1 Cognitive development among institutionalised children

Numerous papers have been published as early as in the 1930's, invariably showing low IQ and language delays among institutionalized children[2] . For the sake of the present review, we focused on the meta- analysis published by van IJzendoorn and colleagues in 2008, combining 75 studies with more than 3,800 children in 19 countries[24] . Mean IQ/DQ was 84+/- 16.8 among institutionalized children, as compared to 104+/- 13 among children raised in families. The mean effect size was an IQ/DQ reduction of 0.75 standard deviation, which is considered a large Cohen's D effect size. The mean difference of 20 points IQ was highly significant and it practically meant that many more children were in the range of mental retardation. Favorable caregiver-child ratios appeared to have a protective effect, whereas longer stays in institutions had a detrimental effect on IQ/DQ. One or more years of family life prior to institutionalization provided a partial protective effect[24] . Children placed in orphanages before 12 months of age did poorer than children reared at home for at least 12 months before being placed in orphanages.

The very unique randomized, controlled Romanian study where institutionalized children were randomized to continue in children's homes, or joining foster care, has provided further important insight into the potential effects of institutionalization. In general, toddlers reared in children's homes had serious intellectual delays, with a mean intelligence at the "borderline-mental retardation" range**.** The children randomized to foster care exhibited significant intellectual gains. Importantly, and consistent with the meta- analysis, the younger the age of joining foster care, the better was the cognitive outcome at 54 months of age[25] . However, according to van IJzendoorn[24] , based on the available data the full extent of the benefits of adoption are still unclear, because adopting parents may tend to choose to adopt better developed children.

In further research, van IJzendroorn et al addressed more closely the question whether the cognitive development of adopted children is different from that of children who have remained in institutional care or in their birth families, or from their current (environmental) non adopted siblings or peers[26] . In a meta-analysis of 62 studies including 17,767 adopted children, the team compared their current non- adopted environmental peers or siblings. Adopted children showed similar IQ scores but their school performance and language abilities lagged somewhat behind[26]. Importantly, there was a twofold increase in special-education referrals among adopted children compared to their non-adopted peers. These results indicate a positive impact of adoption on children's cognitive development with adopted children showing remarkably normal cognitive competence but somewhat delayed school performance.

6.2 Prevalence of FASD among institutionalized children

It has been estimated that over 600,000 children reside in children's homes in Russia. Miller et al reported, in a phenotypic survey, on the rate of FASD among children residing in Russian orphanages[21] . They screened 234 toddlers at a mean age of 21months (SD 12.6), including facial dysmorphology, other physical signs and growth rate. The medical charts of 54% of the cases were also reviewed. Thirteen percent of children had facial dysmorphology highly compatible with FASD, and 45% had intermediate dysmorphology. The facial dysmorphology correlated with reduced physical growth and developmental delay. More than 70% of children with high pre- defined FASD phenotypic scores exhibited moderate to severe developmental delay.

Lange et al. conducted a meta- analysis of the prevalence of FASD among institutionalized children. The overall pooled prevalence was 6% (60 per 1,000, 95% CI 38-85) for full blown FAS, and 16.9% (95% CI 109-238 per 1,000) for the whole range of FASD[27] .

The same group completed an additional meta-analysis on the prevalence of FASD among "children in care" [28]. Overall, 69 studies included 6,177 individuals diagnosed with FASD from 17 countries. The estimated prevalence of FASD was 10-40 fold higher than the 7.7 per 1000 in the general population. The top prevalence was in Russia, with a pooled prevalence of 95. 5 per 1,000 (95% CI 85.3-105.4). Prevalence was lower in other countries, but still very high in comparison to normal populations[28] .

VII. INTEGRATING THE EXISTING DATA INTO MEDICAL KNOWLEDGE AND COUNSELING

The goal of the present article was to estimate what are the risks of institutionalized children of not fulfilling normal developmental trajectory.

According to the thorough meta -analysis by van IJzendoorn and colleagues[24] , the typical institutionalized child looses about 20 IQ points. This can be the result of multiple causes, starting from the genetics of the parents, the suboptimal family and institutional physical resources, minimal staffing, extreme neglect, lack of adequate caregiver-child interactions and sometimes malnutrition or nutritional imbalance. In the vast majority of cases there is insufficient information on the medical and psychiatric status of the biological parents. Numerous studies have shown that some of these insults can be reversed by transferring the child to foster or adoptive homes, and comparison of these adopted children to their non-adopted peers reveals an encouraging positive impact of adoption on children's cognitive development [24-26] . In the case of FASD, the prevalence is up to 40 fold higher than in the general population, and the range is up to 45% of all institutionalized children.

In parallel to addressing the information needs of the medical community and parents, these findings should be balanced by more research focusing on potential interventions in affected cases; how institutions should strive to prevent "structural neglect"; and how institutions should deal with children with FASD.

One cannot over emphasize the importance of diagnosis of FASD which can help foster and adopting parents to adequately support the child. Not knowing that the child is affected by FASD would implicate that the child might not receive the attention and support needed. Therefore adequate methods for diagnosis are necessary.

The examining physician dealing with institutionalized children should carefully assess the gestational age at delivery and birth weight, look for any dysmorphic features or aberration of postnatal growth, and above all, should carefully assess the developmental and behavioral milestones, evaluating their adequacy for the child's chronological age. The examiner should keep in mind that often institutionalized children tend to be behind in their developmental milestones and that developmental milestones can normalize if the child is raised in a favorable environment[19,20] . If one suspects FASD or genetic diseases which may be in the differential diagnosis of FASD[29] , a complete genetic evaluation can be carried out including chromosome studies, chromosomal microanalysis (CMA), exome sequencing or complete DNA sequencing. It is as yet impossible to diagnose all neurodevelopmental problems but the many that can be diagnosed should be explored.

VIII. CONCLUSIONS

Comparison of adopted children after institunalization to their non-adopted peers reveals a very encouraging positive impact of adoption on children's cognitive development, with comparable cognitive achievements, and this milestone should be used to ensure that their innate potentials are met and fulfilled.

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Author Contributions:

GK conceived the project, executed the search and wrote the first draft . AO wrote the section related to other drugs of abuse.

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Comparative Assessment of Three Toothpastes and Prophylactic Polishing Paste as A Method of Iron Stain Removal in Primary Teeth: An in-Vitro Study

Dr. Devendra Patil, Dr. Komal Nanavati, Dr. Monica Yadav, Dr. Shantanu Deshpande, Dr. Aishwarya Kamble & Dr. Farhin Katge

ABSTRACT

Aim: To compare and assess the efficacy of three toothpastes compared to prophylactic polishing paste as iron stain removal method in extracted primary teeth.

Method: Sixty extracted primary anterior teeth were decoronated at cementoenamel junction, followed by filling the pulp chamber with flowable composite. The teeth were then immersed in ferrous sulphate solution and digital images were obtained. The teeth were subjected to electric tooth brushing using Colgate® Visible White (Group A), Himalaya® Sparkling White (Group B) and Biomed® Superwhite (Group C) toothpastes. Prophylactic polishing paste (Group D) was used as control for stain removal. Post-intervention digital images were obtained and color parameter differences (L*, a*, b *, hue, chroma and ΔE) were evaluated using image color summarizer software. The data was then statistically analysed using one way ANOVA test. Intergroup analysis was done using bon ferroni multiple comparison test.

Results: Significant differences in L* and b* colour parameters were obtained for Group A, B and D ($p < 0.05$); however, a* parameter did not show a significant change in values for any group. A significant difference was observed in terms of chroma in groups A, C and D. No significant difference was observed in hue parameter values for all four groups. Intergroup comparison of ΔE revealed significant differences between groups D ($p < 0.05$) and group A, B and C respectively.

Keywords: extrinsic dental stain, iron, primary teeth, dentifrices.

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Conclusion: A regular dental prophylaxis remains the best method for iron stain removal in children. Although newer dentifrices for stain removal are available they are not as efficient as dental prophylaxis.

Keywords: extrinsic dental stain, iron, primary teeth, dentifrices.

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I. INTRODUCTION

Esthetic dentistry is an essential component in modern dental practice. Dental esthetics exerts a key role in a person's self-image, confidence and personality.[1] In a study by Gupta et al. (2019) it was concluded that children are affected

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psychologically by negative social judgements due to problems in dental appearance.[2] A similar study by Abanto et al (2011) stated that development of abstract thinking and concept of self-image occurs around the age of 6 years. At this time, any disorder related to esthetics may psychologically distress the child due to the judgement of their peers.[3]

One of the various dilemmas in esthetic dentistry is discoloured teeth. Tooth discoloration is broadly divided into two types, discoloration due to intrinsic factors when the inner layer of enamel or dentin becomes discoloured. It is usually due to systemic or congenital causes like blood disorders, ingestion of certain drugs disorders like enamel hyploplasia etc.[4] The other cause is discoloration due to extrinsic factors. Extrinsic discoloration occurs due to the build-up or retention of external stains within the salivary pellicle covering the tooth surfaces by chemical alterations. This build up may be due presence of chromogens in foods and drinks e.g. coffee, tea etc, smoking habit or certain medications.[5]

Iron formulations are routinely prescribed for children younger than 2 years of age to improve iron uptake as well as to help prevent iron deficiency and iron- deficiency anemia.[4] Studies done by Nordbo H et al. (1982)[6], Watts A et al. (2001)[7] and Christofides A et al. (2006)[8] have documented black staining on the teeth of children taking iron supplements in form of syrups, drops or some other preparation. These stains can be easily removed in a dental setup using a low- speed handpiece with a rotary brush and prophylactic polishing paste.

Nowadays, a wide range of dentifrices, which specifically concentrate on the problem of tooth discoloration are available. Most of these products are incorporated with abrasive systems and additional chemical agents that supplement abrasive action. These agents prevent stain build-up by using a physical mode of action to remove stains during tooth brushing.[9] Few such readily available dentifrices are Colgate® Visible White, Himalaya® Sparkling White and Biomed® Superwhite toothpaste which have been used in this study. Colgate® Visible White contains silica and pyrophosphate which help in prevention of surface staining due to plaque formation. Himalaya® Sparkling White toothpaste contains papaya and pineapple extracts. These extracts render papain and bromelain which help in whitening of teeth. Biomed® Superwhite toothpaste contains bromelain, a pineapple extract that aids in stain reduction. These newly introduced whitening toothpastes could be used at home for the removal of iron stains.

Hence, the aim of this in vitro study was to compare and assess the efficacy of three toothpastes (Colgate® Visible White, Biomed® Superwhite, and Himalaya® Sparkling White) compared to prophylactic polishing paste as iron stain removal method in extracted primary teeth.

II. MATERIALS AND METHODS

2.1 Sample size

Sample size was determined in concordance to results from a previous study[4] through G* power software (version 3.0.10 with alpha at 0.05 and beta at less than 0.2 (power > 80%). The total sample size calculated was 60 (15 per group).

2.2 Ethical approval

Approval of the study was obtained from the Institutional review Board Ethics Committee (IRB-EC), protocol approval number isTDC/EC/14/2020.

2.3 Preparation of samples

Sixty primary anterior teeth extracted due to physiologic mobility or orthodontic reasons were included in the current study. Any teeth with caries, restorations, developmental defects, enamel cracks, or external discoloration were excluded. The teeth were cleaned manually to remove the soft tissue residue from the surface following which they were stored in sterile 0.9% saline at room temperature till further use.

All the teeth were immersed in 5.25% sodium hypochlorite solution (Chloraxid 5.25%, PPH Cerkamed Wojciech Pawlowski, Poland) for 30 minutes. After rinsing the teeth were cut at the cementoenamel junction (CEJ) and the pulp chamber was cleared of all the remnants using a high speed handpiece and round bur. The prepared pulp chamber was air dried followed by etchingwith 36% phosphoric acid (Blue Etch 36% phosphoric acid, PPH Cerkamed Wojciech Pawlowski, Poland) for 30 seconds. Bonding agent (3M Single bond universal adhesive, Neuss, Germany) was applied after rinsing and drying the pulp chamber,and light cured for 20 seconds. Flowable composite (Beautifil Flow, Shofu INC. Kyoto, Japan) was injected in the pulp chamber and light cured using Ivoclar Vivadent Bluephase N M Light Cure Unit (New York, USA) for 20 seconds. The teeth were then placed in ferrous sulfate solution (Tonoferon drops, East India pharma works Ltd., India) for 30 hours for the purpose of staining. The stained teeth were randomly divided into four groups (n= 15) corresponding to the mode of intervention for stain removal.

The teeth were mounted on a block and positioned inside a light box containing a single light source and photographed using a digital camera (Canon 1300d: 11 aperture, 1/8th shutter speed and 400 ISO film speed) against a green background for pre-intervention images. The digital camera was fixed at a 20 cm distance from the specimen surface, onto a tripod that was placed on the ground. The method and angulation of lighting and photography were maintained the same for all specimens. Once the images were obtained, they were then transferred to a computer.

The four groups used in the current study were:

Group A- Colgate® Visible White toothpaste (Colgate- Palmolive India Ltd., Mumbai, India)

Group B- Himalaya® Sparkling White toothpaste (Himalaya Herbal Healthcare, Bengaluru, India)

Group C- Biomed® Superwhite toothpaste (Organic Pharmaceuticals, LLC, Novgorod region, Russia)

Group D- Glaze prophylactic polishing paste (control group).

2.4 Brushing apparatus

A custom made brushing apparatus was constructed using the handle of powered toothbrush fixed into a customized plastic box packed with dental plaster mould. (Figure 1) The teeth in Group A, Group B and Group C were brushed using Oral-B® CrossAction Power-Battery Powered Electric Toothbrush (Oral-B, P&G, Ohio, USA). A solution was prepared by dissolving 15 g of the toothpaste in 45mL of water, for each group.[10] The toothbrush was mounted in the customized mould with a tooth specimen fixed beneath it. (Figure 1) The brushing was done for two minutes for each specimen. A separate toothbrush head was used for each group. In Group D, all the teeth were subjected to prophylaxis using a prophylactic rotary brush and paste (glaze polishing paste) with a low speed hand piece (NSK Corporation, Japan).

Digital photographs were repeated under the same conditions for all the specimens.

2.5 Software analysis of iron stain removal

The pre and post- intervention images (Figure. 2,3) were transferred to a computer and evaluated using image color summarizer software (Image Color Summarizer 0.76 © 2006-2020 Martin Krzywinski http://mkweb.bcgsc.ca/color-summarizer/?analyze). This software gave the R (red), G (green) and B (blue) values for the images. The RGB values were converted into L* [for the lightness/ luminosity from black (0) to white (100)], a* [from green (–) to red (+)] b* [from blue (–) to yellow (+)] parameters using the CIELAB converter in colormine software (ColorMine library, open- source, MIT licensed .NET project. http://colormine.org/convert/rgb-to-lab). The L (value), C (chroma), and H (hue) parameters were obtained using RGB to LCH converter in the colormine software. ΔE (the

difference in the Lab parameter between two different points in the colorspace) was calculated using the same colormine software.

2.6 Statistical analysis

Data obtained was tabulated and analysed statistically. The differences in the treatment groups in terms of changes in the L*, a*, b*, C, Hand ΔE parameters were analyzed using one-way ANOVA. In cases for which the results of ANOVA became significant, inter group comparison was carried out using bon ferroni multiple comparison test. Statistical analysis was performed using SPSS® software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

III. RESULTS

A total of 60 primary anterior extracted teeth were included in the study. In group A (Colgate Visible White toothpaste) pre-intervention values for L*, a*and b* were 84.79 ± 2.87, 1.41 ± 1.06 and 18.74 ± 2.84 whereas post intervention (brushing the samples with the toothpaste) values for L*, a* and b* were 89.35 ± 3.10,1.41 ± 1.06, and 17.98 ± 9.98, respectively. A significant difference between pre and post-interventions values was observed in the L* and b*parameters. ($p<0.05$).

In group B (Himalaya Sparkling White toothpaste) pre-intervention values for L*, a*and b* changed from 75.48 ± 2.45, 2.68 ± 1.83 and 21.66 ± 5.27 to post-interventions values, 78.87 ±3.11, 3.03 ± .95, and 22.85 ± 3.93 respectively. No significant difference was observed in the pre and post-intervention values of any parameters for this group.

In group C (Biomed Superwhite toothpaste) pre-intervention values for L*, a* and b* changed from 76.14 ±4.22, 2.89 ± .74 and 23.14 ± 4.30 to post-intervention values, 80.40 ±3.03, 2.49 ± 1.42 and 22.98 ± 3.17, respectively. The difference between pre and post-interventions values for the L* and b* parameters was found statistically significant. ($p<0.05$)

In group D (prophylactic polishing paste), pre intervention values for L*, a* and b* changed from 71.75 ±4.24, 3.02 ± .70 and 22.08 ± 2.26to post-intervention values, 83.25 ±4.23, 1.19 ± .90 and 23.63 ± 3.95, respectively. A significant difference was observed between pre and post-intervention values for L* and b* parameters. ($p<0.05$) (Table 1)

Hence, significant differences ($p<0.05$) in the L* and b * color parameters can be seen for group A, B and D; however, the difference in the pre and post-intervention values of a* parameter did not show a significant difference for any group.

With regard to the LCH parameter Group A, hue (H) value changed from 85.59 ± 3.16 to 89.06 ± 4.16 and chroma (C) from 18.82 ± 2.85 to 17.95 ± 3.87, and value for L being the same with L*, hence it was not mentioned again. In group B, hue (H) value changed from 84.52 ± 4.17 to 81.94 ± 3.19 and chroma (C) from 24.26 ± 4.88 to 22.89 ± 3.76. In group C, the hue (H) of the samples changed from 83.06 ± 2.00 to 83.71 ± 3.35 and chroma (C) from23.61 ± 4.21 to 23.15 ± 3.19. In group D, the hue (H) values changed from 82.18 ± 1.85 to 87.00 ± 1.89 and chroma (C) from 22.30 ± 2.27 to 23.67 ± 3.97. A statistical significant difference was observed in terms of the chroma in groups A, C and D. ($p < 0.05$) No significant difference was observed in the terms of changes in hue for all the four groups. (Table 1)

The mean ΔE values for sample teeth in the four groups were 5.28 ± 2.14, 4.62 ± 2.88, 5.07 ± 2.73, and 12.48 ± 5.23, respectively. One-way ANOVA revealed significant differences in the range of changes in ΔE values among different toothpaste groups.($p < 0.05$) (Table 2) Considering the significant results for ΔE values, intergroup comparison in this regard was carried out. Intergroup comparison of ΔE values revealed significant differences between group A, B, C and D respectively. ($p < 0.05$) (Table 3).

IV. DISCUSSION

Black extrinsic tooth stains have a prevalence of 1 to 20% in children. They are characterized by dark lines or incomplete amalgamation of dark dots on the cervical third of enamel.[11] The pellicle layer is a proteinaceous organic film on tooth surface and also serves as a protective barrier. It also acts as a substrate for bacterial growth which ultimately leads to formation of dental plaque and has the tendency to absorb pigments causing extrinsic stains on teeth.[12] Reid et al. (1977) suggested that the cause of pigmentation in children's teeth was probably ferric sulphide, formed by the reaction between hydrogen sulphide produced by bacteria and iron in the salivary or gingival exudate. Black stain influences the esthetics of teeth and is difficult to remove with a regular dentifrice and toothbrush.[13] Therefore the present study evaluated the iron stain removal efficacy of Colgate® Visible White, Himalaya® Sparkling White and Biomed® Superwhite dentifrices in comparison with dental prophylactic polishing paste.

The stain removal efficacy can be assessed by visual assessment with shade guides and indices. Digital assessment can be done using techniques such as colorimetry and spectrophotometry which measures the color changes after intervention in teeth. Computer analysis of digital images can also be done to assess the efficacy of stain removal. Digital images offer an objective shade difference value and are very sensitive for minor changes in stain removal. A standardized method must be employed in relation to camera, light and positioning of the teeth.[14] Hence, in present study all digital equipment including camera, software, lighting and positioning of teeth were standardised increasing the accuracy of the study.

The current study measured L*, a*, b * and LCH color parameters. In the terms of LCH parameters L* is the degree of lightness and the values are same as L* parameter in the Lab system. In accordance with the Munsell color chart, color has three parameters hue, value, and chroma. Hue (H) is the perception of observer from the color and depends on different wavelengths of light beams that reach the eyes. Value (L) is the achromatic dimension of color and indicates its lightness or darkness. Higher the value, lighter the color and lower the value, darker the color. Chroma (C) is the intensity of color. A greater the value of chroma means more richness in the color.[15]

Nowadays, a vast selection of dentifrices are available in the market, specifically addressing removal of pellicle associated extrinsic stains. These dentifrices include higher quantities of abrasives and detergents; in order to remove tough stains.[16] Different abrasivity of toothpastes depends on the hardness, shape, size and amount of the abrasive particles in the toothpaste. The active ingredients in a dentifrice include enzymes that dissolve pellicle proteins or chelating agents that have stain-dissolving properties. Alumina, dicalcium phosphate dihydrate, silica, calcium carbonate, and calcium pyrophosphate are some of the abrasives that are included in whitening toothpastes.[17]

In the current study, Colgate® Visible white was used. The abrasive agent present in Colgate® visible white consists of silica and polyphosphates. The cleaning efficacy of silica is similar to the abrasive materials used for cleaning and polishing as it physically removes surface stains. The polyphosphates are commonly used to prevent surface staining due to plaque formation.[13] The changes in L* and b* parameter values for iron stain removal using Colgate® visible white, in the current study were statistically significant which may be explained due to the different abrasive contents of the dentifrice. This is similar to the results obtained in the studies by Gerlach et al.[18], Horn et al.[19] and Ghassemi et al.[20] who tested whitening dentifrices, and obtained satisfactory results regarding changes in tooth coloration. They concluded that these results may have been due to the presence of high performance abrasive agents contained such as silica, during the use of these toothpastes.

Biomed® Superwhite dentifrice used in the present study contains pineapple extract bromelain which helps clean enamel of dental plaque. The other ingredients include calcium phosphate polishes the enamel. Himalaya® Sparkling white toothpaste contains papain and bromelain which are proteolytic enzymes as tooth whitening agents. They disrupt and remove the protein portion of the pellicle layer thus removing the stains that are bound to these proteins. Papain is a natural enzyme, derived from latex of the Papaya fruit (Carica papaya). It is known to possess the ability to hydrolyze large proteins into smaller peptides and amino acids.[21] Bromelain is extracted from the stem and fruit of Pineapple (Ananascomosus) plant.[22] In the current study a significant difference was observed in the L* and b*parameters for Biomed® Superwhite toothpaste whereas no significant difference was observed in the pre and post brushing values in any parameters for Himalaya® Sparkling white toothpaste. In studies reported by Kalyana et al.[10], and Patil et al.[23], the ability of these proteolytic enzymes was demonstrated. They used a control dentifrice as Colgate® regular, since the relative dentine abrasive value was nearly the same as test dentifrice containing proteolytic enzymes. A significant increase in the mean L* values for the test dentifrice group could partly be attributed to these enzymes. Another clinical study using toothpaste containing a mixture of papain, alumina and sodium citrate (Rembrandt) has also reported a significant stain removing property.[24]

In the current study Colgate® Visible White showed the greatest ΔE after prophylactic paste and was found to be more efficient than the other toothpastes. Colgate® Visible White and Biomed® Superwhite toothpastes were more effective in improving tooth color and removing stains than Himalaya® Sparkling white toothpaste. The use of toothpastes with a toothbrush enables a benefitting action from both the abrasiveness of toothbrush and the physicochemical properties of toothpaste in stain removal. The decreased intensity of stains may also occur due to narrowing of the stain layer owing to this abrasive action.[4]

Dental prophylaxis is a commonly used technique to remove stains, dental plaque and calculus. However it requires an office visit. The abrasives in the prophylactic paste clean stains on the tooth surface which results in a whitening effect.[24] In the current study all interventions caused color changes in teeth, but prophylactic polishing paste was the most effective as compared to all other groups.

Limitations of the study were smaller sample size and lack of consideration regarding interaction with saliva and various other food substances in the oral cavity. The study of specimens in the clinical setting would be more advantageous. More research is recommended in relation to the oral environment.

V. CONCLUSION

The maximum stain removal efficacy was demonstrated by prophylactic polishing paste as compared to other three commercial toothpastes available in market. Therefore it is recommended that a regular dental prophylaxis serves a dual purpose of iron stain removal in children taking iron supplements and for the maintenance of dental and gingival health.

VI. FUNDING

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VII. COMPETING INTERESTS

Conflicts of interest: There are no conflicts of interest.

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Table 1: Pre and post-intervention values for all four groups.

Group	Parameter	Mean ± Std. Dev.		p Value
		Pre-intervention	Post- intervention	
A (Colgate Visible White)	L*	84.79 ± 2.87	89.35 ± 3.10	.036¶
	a*	1.41 ± 1.06	.21 ± 1.05	0.104
	b*	18.74 ± 2.84	17.98 ± 9.98	0.003¶
	H	85.59 ± 3.16	89.06 ± 4.16	.061
	C	18.82 ± 2.85	17.95 ± 3.87	.002¶
B (Himalaya Sparkling White)	L*	75.48 ± 2.45	78.87 ±3.11	0.37
	a*	2.68 ± 1.83	3.03 ± .95	0.394
	b*	21.66 ± 5.27	22.85 ± 3.93	0.181
	H	84.52 ± 4.17	81.94 ± 3.19	.083
	C	24.26 ± 4.88	22.89 ± 3.76	.199
C (Biomed Superwhite)	L*	76.14 ±4.22	80.40 ±3.03	0.027¶
	a*	2.89 ± .74	2.49 ± 1.42	0.932
	b*	23.14 ± 4.30	22.98 ± 3.17	0.004¶
	H	83.06 ± 2.00	83.71 ± 3.35	.742
	C	23.61 ± 4.21	23.15 ± 3.19	.005¶
D (Prophylactic polishing paste)	L*	71.75 ±4.24	83.25 ±4.23	0.026¶
	a*	3.02 ± .70	1.19 ± .90	0.664
	b*	22.08 ± 2.26	23.63 ± 3.95	.002¶
	H	82.18 ± 1.85	87.00 ± 1.89	.063
	C	22.30 ± 2.27	23.67 ± 3.97	.002¶
¶ denotes significant p value (p<0.05)				

Table 2: Mean ΔE (color difference) values for all four groups.

			95% Confidence Interval for Mean		
Group	Mean ΔE	Std. Dev.	Lower Bound	Upper Bound	p Value
A (Colgate Visible White)	5.28	2.14	3.75	6.82	
B (Himalaya Sparkling White)	4.62	2.88	2.56	6.69	
C (Biomed Superwhite)	5.07	2.73	3.12	7.02	0.001¶
D (Prophylactic polishing paste)	12.48	5.23	8.74	16.22	
Total	6.86	4.67	5.37	8.36	
¶ denotes significant p value ($p<0.05$)					

Table 3: Inter-group analysis using bon-ferroni test for ΔE.

Groups	Colgate	Himalaya	Biomed	Prophy paste
A (Colgate Visible White)	-	1.00	1.00	0.000¶
B (Himalaya Sparkling White)	1.00	-	1.00	0.000¶
C (Biomed Superwhite)	1.00	1.00	-	0.000¶
D (Prophylactic polishing paste)	0.000¶	0.000¶	0.000¶	-
¶ denotes significant p value ($p<0.05$)				

Figure Legends:

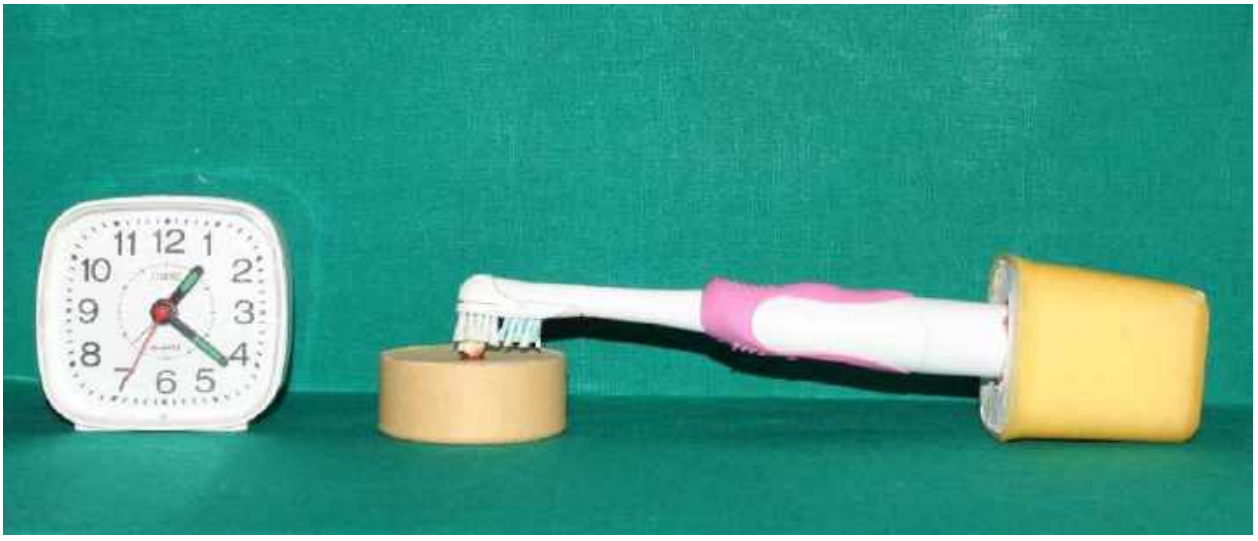

Fig. 1: Brushing apparatus used for stain removal

Fig.2: Pre-intervention digital image used for analysis of tooth in Group D

Fig.3: Post-intervention digital image used for analysis of tooth in Group D

Factors Influencing to Becoming a Blood Donor in Mongolia

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ABSTRACT

Background: Blood donated by donors saves the lives of many millions of people. Because of the development of medical science and population growth the demand for blood and blood components is increasing throughout the world.

Goal: To define social and cultural factors influencing the population to become voluntary non-remunerated donors Materials and methods: We used a questionnaire for defining influencing factors on blood donation and randomly selected 7633 adults to enroll in the survey from urban and 4 rural provinces. For the data analysis, we used a SPSS software version 21. Results were expressed by percentage of age of knowledge, attitude and average indicators among the population and used corresponding statistical tests. Qualitative survey methods were also used for obtaining the data.

Results: Average age of the respondents is 36.4, majority of them had higher education (40.8%), and completed secondary education (28.9%), khalkh (84.8%), and married (63.1%). As for survey site locations, most respondents were from urban (64.0%, 4887), most of them were Buddhists (51.9%). 14.6% survey respondents were blood donors who are living in urban areas, female, between 18-35 years of age, with completed high education, and married. 45.4% of them decided to donate blood by their own will. To help someone and save a life are the main reasons for blood donation. Respondents failed to donate their blood because family not allowed, afraid, risk of infection, doesn't want to be busy.

Keywords: blood donation, factors to become a blood donor.

Classification: NLMC Code: WH 460

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Conclusion: The main factors to becoming a blood donor are education level, gender, attitude of working environment, and willingness to do good deeds.

Keywords: blood donation, factors to become a blood donor.

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I. INTRODUCTION

Blood transfusion saves lives and improves health, but many patients requiring transfusion do not have timely access to safe blood. Providing safe and adequate blood should be an integral part of every country's national health care policy and infrastructure[1].

[1] WHO, 2019, Blood safety and availability, https://www.who.int/en/news-room/fact-sheets/detail/blood-safety-and-availability

WHO estimates that blood donation by 1% of the population is generally the minimum needed to meet a nation's most basic requirements for blood; the requirements are higher in countries with more advanced health care systems. However, the average donation rate is 15 times lower in developing countries than in developed countries. Globally, more than 70 countries had a blood donation rate of less than 1% (10 donations per 1000 population) in 2006[2]. Voluntary blood donors, particularly regular donors, are the first line of defense in preventing the transmission of HIV, hepatitis viruses and other blood borne infections through the route of transfusion. A number of studies have reported significantly lower prevalence of transfusion transmissible infection markers among voluntary donors compared with other types of donors, with the lowest rates among regular donors[3].

Blood donors are committed to social responsibility, saving lives and improving the health of others. In Mongolia, the legal environment on blood donation has been well established and the national blood bank is consistent with solely blood donated by donors. The necessity for blood and blood products in Mongolia is getting higher and higher every year which probably is associated with high-mortality-rate diseases. It has been estimated that about 100 blood donors donate blood would convince the necessity of blood in Mongolia.

In 1994, Mongolia conducted a new donor system and in 2018 January 19th the government renewed the previous blood donor law. The updated law improved the legal environment for blood safety. The number of blood donations increased from 16707 in 2013 to 25602 in 2017 by 53%, 5932 in 2013 to 7805 in 2017 by 31.5% in the National Center Blood Transfusion Medicine and Blood service centers respectively. The percentage of donors increased from 37.2% to 55% in 2017. However, till now desired blood products are limited and number of permanent blood donors are not sufficient in current demand of blood products.

In 2007, Mongolian Parliament passed a resolution No.45 on "Policy to Ensure Improvement and Safety of Donor Blood and Blood Products Supply" which indicates that the supply of safe blood and blood component is an issue at the center of the government's attention. This policy has defined the methods to implement the main direction of the activities to ensure a sufficient supply of safe and quality blood and blood components with proven efficacy for the continuous operation of health facilities even during national disasters. In 2008, the Government of Mongolia issued a resolution No. 111, an action plan to implement the Policy on "Improvement of Supply and Safety of Donated Blood and Blood Products".

To ensure safe sufficient blood and blood products are essential in Mongolia. Thus, we had evaluated the level of knowledge, attitude and practice towards voluntary blood donation among the general population and determined factors which could influence becoming a permanent blood donor.

Goal:
To define social and cultural factors influencing the population to become voluntary non-remunerated donors.

II. MATERIALS AND METHODS

In 2019, conducted a survey of volunteer community whole-blood donors to evaluate motivations for giving blood. The self-administered survey questionnaire included questions regarding donation history, knowledge and attitude about blood donation, intention to return, donation experience, and motivating factors.

[2] WHO Blood Safety Indicators, 2007. Geneva, World Health Organization, 2009.
[3] WHO and IFRC, 2010, Towards 100% voluntary blood donation: a global framework for action, World Health Organization and International Federation of Red Cross and Red Crescent Societies. ISBN 978 92 4 159969 6

2.1 Survey scope:

The minimum need of the country is met when 1 or more percent of the adult population of Mongolia becomes regular non-remunerated blood donors. Therefore, the scope of the survey covered knowledge, attitude and practice of a represen- tative sample of the Mongolian population aged between 18-60 on non-remunerated blood donation and factors influencing them.

2.2 Questionnaire based research:

The knowledge, attitude and experience of blood donation and factors influencing decision-making are identified through interviews using pre-developed questionnaires.

2.3 Qualitative research:

Individual and focus group discussions were used to clarify difficulties and factors influencing decision-making to donate blood for first and multiple time blood donors. This reveals the reasons why the adult population of eligible age between 18-60 years does not become voluntary non-remunerated donors.

2.4 Survey population, size of the sample and selection:

The survey covered a population aged 18-60 years in 5 provinces and 6 districts of Ulaanbaatar city. Population of the age of 18-60 years was randomly selected by the survey. Because the Kazakh population represents 3.9% of the total population, Bayan-Ulgii aimag was selected in the targeted sampling in order to identify whether cultural and religious reasons have an impact on blood donation. Four central districts and 2 remote districts were selected in Ulaanbaatar City by targeted sampling. The selection considered population density, disease burden, and distance from Ulaanbaatar city. When determining the sample size the level of knowledge, attitude and practice among the population on blood donation is considered as 50.0% with a probability of 95% (Z=1.96), standard deviation (p=0.05), complex sample impact coefficient (1.5) of gender balance and living location representativeness in all age groups (4 age groups for each gender, in total 8). Based on these principles the survey covered a total 6876 people. The number of people who might refuse to participate was considered 10 percent and this was added to the total number of people making a total of 7564 (Formula 1).

2.5 The formula 1 used for estimating the size of the sample:

$$n = Z^2 \frac{P(1-P)}{e^2}$$

$$n = 1.96^2 \frac{0.46(1-0.46)}{0.0025} = 3.8416 \frac{0.2484}{0.0025} = 381.70$$

n x complex sample coefficient x age x gender = 382 x 8 x 1.5 x 1.5 = 6876

The households were randomly selected based on the revised population census corresponding to the adult population of selected province centers and smallest unit of government.

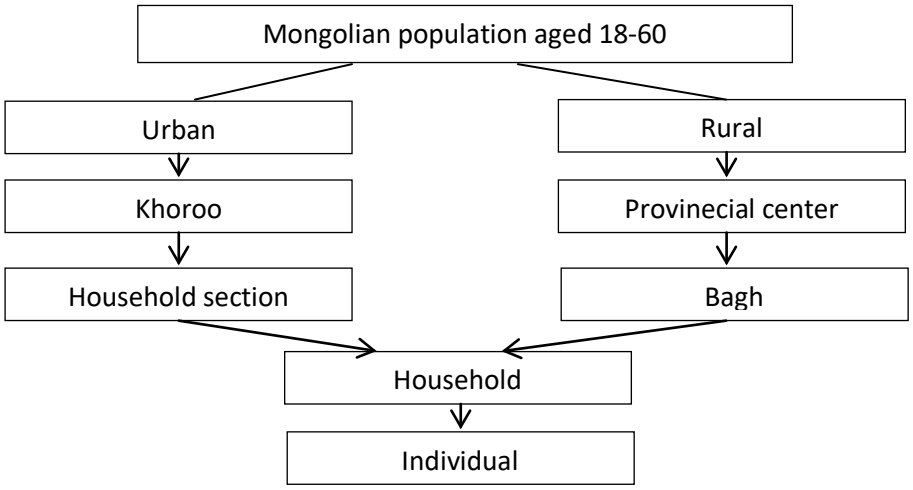

Figure 1: Phases of multiple phase random sampling

The ultimate unit of the sampling or the individual were randomly selected using Kish method among people aged 18-60 from members of selected households. One adult of a selected household was covered by the survey (Figure 1).

In order to ensure that the population of Mongolia is represented the survey sample was selected by multiple phase selection method. In order to ensure a proper ratio between the urban and rural population the survey sampling was done separately in each city. Also we had conducted several in-depth interviews and focus group discussion with selected survey respondents.

III. DATA PROCESSING

Statistical analysis SPSS version 21 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Results were expressed by percentage of knowledge, attitude and average indicators among the population. Confidence interval of 95% (95% CI) was used to identify differences in results' accuracy indicators (distribution percentage) and groups (age, gender, location).

The prevalence of measurement and general tendency of the blue spot and outcome measures (prevalence and mean variance) and differences between groups (gender, age, location, and ethnic group) were calculated with 95% confidence internals (95%CI). The relevant parametric and nonparametric tests such as Mann-Whitney U test, Chi square, Kruskal-Wallis, and in order to determine normality of the variance we used the Kolmogorov –Smirnov test.

IV. RESULTS

The survey covered a total 7633 people and the respondent coverage rate was 100%. Table 1 shows the social and demographic indicators of the respondents.

The table 1 shows that average age of the respondents is 36.41 [36.09-36.73], majority of them were had higher education (40.8%, 3115), and completed secondary education (secondary and high) (28.9% 2204), khalkh (84.8%, 6472), married (63.1%, 4818), and single (28.7%, 2194). As for survey site locations, most respondents were from urban (64.0%, 4887), as for religion most of them were Buddhists (51.9%, 3960) and atheists (29.9%, 2281).

The average number of family members is 4.18 [4.15-4.21] and the largest number was 11 members. Totally (88.8%) gave their household income. The average household income level was 800,000±488,419 [95%CI: 800000-851713] MNT. The smallest income level was 100,000 MNT, the highest level was 4,500,000 MNT. In general, social indicators of these respondents are similar to the Mongolian population statistics.

This indicates that the study sample represents the Mongolian population aged 18-60. Demo-

graphic indicators of respondents were similar to statistical indicators of Mongolia which means the sample of the survey is representative of the general population of Mongolia in terms of showing their knowledge, attitude, and practice.

Table 1: Some social and demographic characteristics of the respondents

Social and demographic characteristics	Male (% and 95%CI)	Female (% and 95%CI)	Total number of respondents (% and 95%CI)
Living location			
Urban	2139 (62.2)	2748 (65.5)	4887 (64.0)
Rural	1298 (37.8)	1448 (34.5)	2746 (36.0)
Education level			
Uneducated	57 (1.7)	65 (1.5)	122 (1.6)
Only literate	9 (0.3)	4 (0.1)	13 (0.2)
Primary	105 (3.1)	83 (2.0)	188 (2.5)
Secondary	497 (14.5)	491 (11.7)	988 (12.9)
Secondary and high	1056 (30.7)	1148 (27.4)	2204 (28.9)
Vocational	405 (11.8)	391 (9.3)	796 (10.4)
Bachelor	1226 (35.7)	1889 (45.0)	3115 (40.8)
Master, PhD	82 (2.4)	125 (3.0)	207 (2.7)
Marital status			
Single	1042 (30.3)	1152 (27.5)	2194 (28.7)
Married	2153 (62.6)	2665 (63.5)	4818 (63.1)
Living with a partner	98 (2.9)	133 (3.2)	231 (3.0)
Separated	52 (1.5)	76 (1.8)	128 (1.7)
Divorced/widow	92 (2.7)	170 (4.1)	262 (3.4)
Mean # of family members	4.20 [4.15-4.25]	4.16 [4.11-4.20]	4.18 [4.15-4.21]
Age group			
Mean age	36.54 [36.12-37.02]	36.30 [35.89-36.70]	36.41 [36.09-36.73]
18-25 years	903 (26.30)	1052 (25.10)	1955 (25.60)
26-35 years	845 (24.60)	1154 (27.50)	1999 (26.20)
36-45 years	786 (22.90)	967 (23.00)	1753 (23.00)
Above 45	903 (26.30)	1023 (24.40)	1926 (25.20)
Ethnicity			
Khalkh	2854 (83.0)	3618 (86.2)	6472 (84.8)
Kazakh	281 (8.2)	305 (7.3)	586 (7.7)
Buryad	153 (4.5)	131 (3.1)	284 (3.7)
Zakhchin	72 (2.1)	54 (1.3)	126 (1.7)
Others	77 (2.7)	88 ()	165 ()
Religion			
Atheists	1170 (34.0)	1111 (26.5)	2281 (29.9)
Buddhism	1675 (48.7)	2285 (54.5)	3960 (51.9)
Christian	87 (2.5)	166 (4.0)	253 (3.3)
Islam	235 (6.8)	244 (5.8)	479 (6.3)
Shamanism	266 (7.7)	389 (9.3)	655 (8.6)
Others	4 (0.1)	1 (0.0)	5 (0.1)
Total	3437	4196	7633

Figure 1 shows the respondents by gender, whether they have a chronic disease or are on some medication. Out of total respondents, 16.6% [95%CI: 15.7-17.4] had any kind of chronic diseases, 16.4% [95%CI: 15.6-17.3] use constant medication (Figure 2).

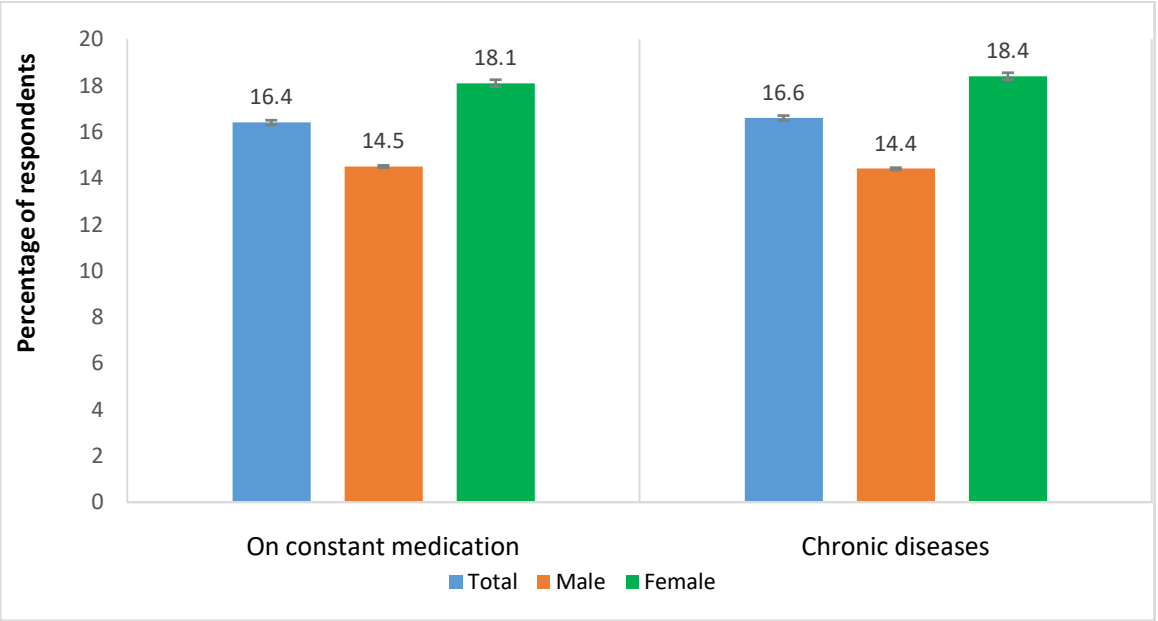

Figure 2: Morbidity of survey respondents, by gender, 2019

Most of (87.3%) all respondents and 86.7% of males have heard about non-remunerated voluntary blood donation. There was no difference between the living location and gender of the population in terms of whether they heard about non-remunerated voluntary blood donation. The survey clarified whether survey respondents had friends, family members, relatives who are blood donors. 59.4% of total respondents, 61.6% of male, 57.6% of female respondents do not know anyone who donates blood 2.8% of males, 3.4% of female respondents were blood donors. Overall 3.2% (n = 241) of survey respondents were blood donors (Table2).

Table 2: Respondents who know a blood donor, by gender

№	Whether the respondent knows a blood donor	Male	Female	n (%)
1.	Do not know anyone	2118 (61.6)	2415 (57.6)	4533 (59.4)
2.	Friends	485 (14.1)	606 (14.4)	1091 (14.3)
3.	Family members, relatives	279 (8.1)	412 (9.8)	691 (9.1)
4.	Co-workers	143 (4.2)	190 (4.5)	333 (4.4)
5.	Ordinary acquaintances	237 (6.9)	343 (8.2)	580 (7.6)
6.	Myself	97 (2.8)	144 (3.4)	241 (3.2)
7.	Other	9 (0.3)	18 (0.4)	5 (0.1)
8.	Cannot tell	73 (2.1)	86 (2.0)	27 (0.4)
	Total	3437 (100.0)	4196 (100.0)	7633 (100.0)

Ninety point two (19.2%) percent of survey respondents [95%CI: 18.4-20.1] said they donated their blood at least once in lifetime. 43.3% out of these people [95%CI: 40.6-46.3] donated only once, 31.9% (95%CI: 29.4-34.6) donated twice.

Table 3: Characteristics of respondents who had donated a blood

Indicators	Age group									
	18-25		26-35		36-45		46 and +		Total	
	n	%	n	%	n	%	n	%	n	%
1. Location, χ^2=10.96, p=0.012										
Rural	110	29.3	122	34.0	139	41.0	136	34.5	507	34.5
Urban	266	70.7	237	66.0	200	59.0	258	65.5	961	65.5
2. Gender, χ^2=11.97, p=0.007										
Male	182	48.4	149	41.5	130	38.3	146	37.1	607	41.3
Female	194	51.6	210	58.5	209	61.7	248	62.9	861	58.7
3. First impressions on blood donation among respondents, χ^2=28.96, p=0.016										
Nice impressions	130	34.6	113	31.5	93	27.4	111	28.2	447	30.4
No special impressions	132	35.1	131	36.5	150	44.2	190	48.2	603	41.1
Thought whether my blood would replenish	42	11.2	37	10.3	37	10.9	27	6.9	143	9.7
Feared of catching an infection	6	1.6	14	3.9	13	3.8	9	2.3	42	2.9
Fear of something	20	5.3	15	4.2	11	3.2	17	4.3	63	4.3
Impression to donate blood again	46	12.2	49	13.6	35	10.3	40	10.2	170	11.6
4. The main reason why blood donors started blood donation χ^2=77.70, p<0.001										
At own will	207	55.1	197	54.9	140	41.3	122	31.0	666	45.4
Compelled to help someone	73	19.4	58	16.2	96	28.3	120	30.5	347	23.6
Needed money	13	3.5	10	2.8	10	2.9	7	1.8	40	2.7
Peer pressure of coworkers	77	20.5	87	24.2	80	23.6	133	33.8	377	25.7
When I was soldier	6	1.6	7	1.9	13	3.8	12	3.0	38	2.6
Total	376	100.0	359	100.0	339	100.0	394	100.0	1468	100.0

Of those respondents who had donated a blood, most of them were aged 36 and above (49.9%, 95%CI: 45.8—54.4), urban citizen (65.5%, 95%CI: 24.8-29.1), and female (58.7%, 95%CI: 56.2-61.3). Some (30.4%) of respondents who donated blood [95%CI: 28.0-32.9] said they had "nice impressions" when first donated blood. 45.4% of people who donated their blood [95%CI: 42.8-47.9] did so at their own free will, 23.6% [95%CI: 21.5-25.8] donated because they were coerced to help someone. 25.7% of survey respondents [95%CI: 23.5-27.9] donated blood following their organization and coworkers.

Also, to help someone and save a life are the main reasons for blood donation. Knowledge of blood donors does not affect the religion or the geographical living place of residence. Most of the people who were interviewed said that they had "nice impressions" when first donating blood (Table 3).

Fourteen point six percent of (14.6%, 95%CI: 11.8-17.6) survey respondents were blood donors. Most blood donors live in urban areas, female, between 18-35 years of age, and with completed high education, and married. Some (37.0%) of these people [95%CI: 27.8-4.4] were donors who

donated their blood once in a year, 34.3% [95%CI:25.9-44.4] of them donate once in 3 months. 61.1% of blood donors of survey respondents [95%CI:51.9-70.4] said that they take blood tests each time when they donate blood, 37.5% of blood donors [95%CI: 27.5-48.7] said that they made somebody from their close circles into a blood donor. 30.6% of them were felt after the first donation to become regular blood donor. Also 45.4% [95%CI: 43.4-54.8] of them decided to donate blood by their own will.

Box 1. First impressions on blood donation among respondents

I have donated my blood to my colleagues. I wasn't planning on doing it regularly but after receiving a healthful text and I have decided to become a regular donor. I have donated my blood 3 times already and plan to do it for a long time.

In-depth interview R, 48 years old female)

Figure 3 shows the reason why blood donors started donating their blood. Most respondents stated that the main reason why they started donating their blood was (59.3%, 95%CI: 50.0-68.5) to do good deeds.

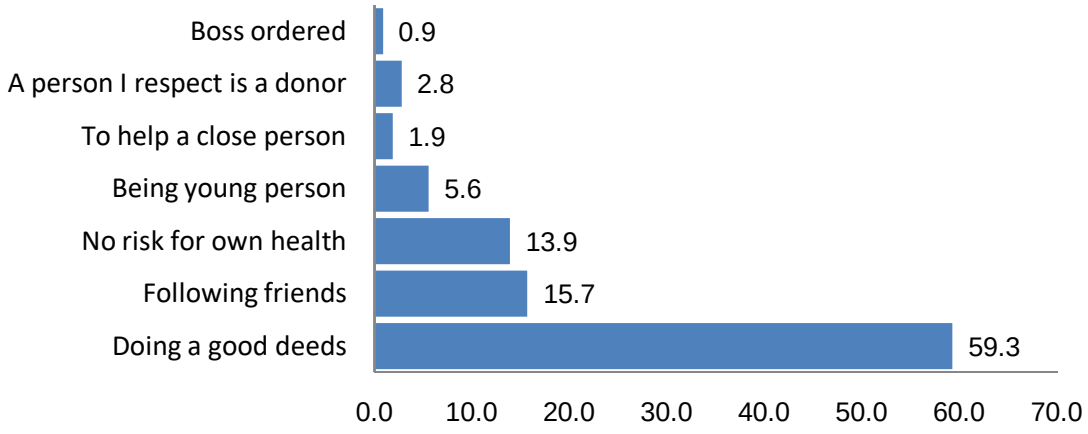

Figure 3: The main reason why blood donors started blood donation, by a percentage of respondents

Blood donors despite saying they are proud to donate blood still expressed their desire to see the Government to support the livelihood and social welfare of blood donors. Blood donors who participated in the qualitative survey appreciated governmental actions such as rewarding blood donors, constantly involving blood donors in any kind of activity in the last years.

Most of the respondents who had a negative attitude toward blood donation live in urban area (63.9% [95%CI: 61.6-66.1]), female (57.2%[95% CI: 54.9-59.6]), uneducated (41.1%[95%CI: 38-5-43.6]), married (56.6% [95%CI: 54.2-58.9]) and khalkh ethnic group (83.7 [95%CI: 81.9-85.4]) of people.

Table 4: General characteristic of survey respondent who believe blood donation has a risk for donors

№	General characteristics of blood donors	Number	%	95%CI
1. Living location				
	Urban	1065	63.9	61.6-66.1
	Rural	602	36.1	33.9-38.4
2. Gender				
	Male	713	42.8	40.4-45.1
	Female	954	57.2	54.9-59.6
3. Educational level				
	Uneducated	73	4.4	3.5-5.4
	Incomplete secondary	9	0.5	0.2-0.9
	Complete secondary	39	2.3	1.6-3.1
	Technical vocational	171	10.3	8.8-11.7
	Higher	457	27.4	25.2-29.5
	Master, doctor	174	10.4	8.9-12.0
	Uneducated	685	41.1	38.5-43.6
	Incomplete secondary	59	3.5	2.7-4.5
4. Marital status				
	Single	549	32.9	30.8-35.2
	Married	943	56.6	54.2-58.9
	Live with a partner	65	3.9	3.0-4.9
	Separated	51	3.1	2.3-3.9
	Divorced/widow	59	3.5	2.6-4.5
5. Ethnicity				
	Khalkh	1396	83.7	81.9-85.4
	Kazakh	159	9.5	8.2-10.9
	Buryad	47	2.8	2.0-3.7
	Zakhchin	25	1.5	0.9-2.1
	Others	40	2.4	1.7-3.2
	Total	1667	100.0	

Almost all quantitative and qualitative survey respondents are considered that donating blood is a good deed.

Box 2. The tendency to consider that donating blood is a good deed

We are ready to help people with the gift of life. It's a wonderful act of kindness.

(From group discussion))

The gift of the body is the best charity. Therefore, I am very happy to be a blood donor.

(In-depth interview)

Majority of the respondents who had a negative attitude toward blood donation (770, 20.4%) thinking of anemia (276, 35.9%), risk of infection (272, 35.4%). 52.2% of people who donated their blood (95%CI: 48.0-56.4) did so at their own will. 93.7% (n 3544) of them were agreed that blood donation is a charity and good work and 93.9% of the respondents (95% CI:93.1-94.7) considered blood donation as a gift of virtue and good deeds. 36.64% of respondents believed that they did not give blood for their blood because they fear of needle, risk of getting any kind of infection, bleeding, or will have low blood volume.

On binary logistic regression, we found that person with sufficient knowledge were more likely to have donated blood before (OR = 3.15, 95% CI

= 3.043.28), along with those in old aged people (OR = 3.71, 95% CI = 3.53-3.92) and living in urban settings (OR = 2.67, 95% CI=2.31-3.05). Details about association between demographics, education and marital status are shown in Table 4-5.

Figure 5 shows risks that might arise when voluntarily donating a blood by the proportion of responses.

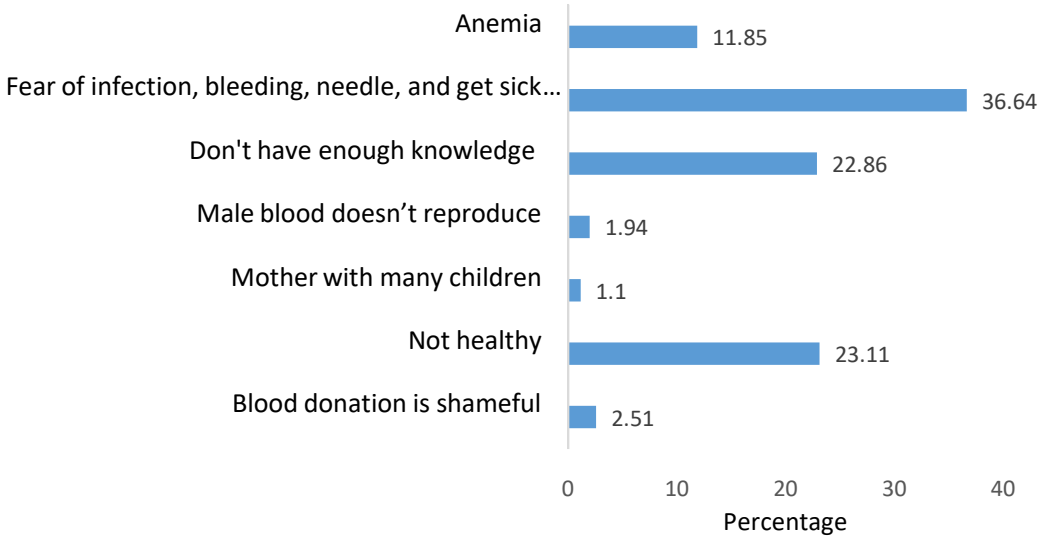

Figure 4: Risks encountered during blood donation, by percentage

The majority of (93.6% [95%CI: 93.1-94.7]) respondents agreed that blood donation is a good deed regardless of gender, education level, religion. But Buddhists, highly educated respondents, female, and aged above 26 years orders are slightly higher than other groups (Table 5).

Table 5: A tendency to consider giving blood as a virtuous act, by gender, age, education, religion

	Agree with blood donation is a good deed	Not agree with blood donation is not a good deed	Total
1. Gender, χ^2=11.97, p<0.001			
Male	3072 (93.1)	229 (6.9)	3301
Female	3802 (94.0)	244 (6.0)	4046
2. Age group, χ^2=35.23, p<0.001			
18-25 years	1651 (90.6)	171 (9.4)	1822
26-35 years	1832 (94.2)	112 (5.8)	1944
36-45 years	1606 (94.5)	93 (5.5)	1699
Above 46 years	1785 (94.8)	97 (5.2)	1882
3. Education level, χ^2=57.57, p<0.001			
Uneducated	94 (79.7)	24 (20.3)	118
Incomplete secondary	11 (84.6)	2 (15.4)	13
Complete secondary	161 (86.6)	25 (13.4)	186
Technical vocational	888 (92.9)	68 (7.1)	956

Higher	1935 (92.7)	153 (7.3)	2088
Master, doctor	749 (95.7)	34 (4.3)	783
Uneducated	2852 (94.9)	153 (5.1)	3005
Incomplete secondary	184 (92.9)	14 (7.1)	198
4. Religion, χ^2=80.2, p<0.001			
Atheists	2017 (91.8)	180 (8.2)	2197
Buddhism	3633 (95.7)	164 (4.3)	3797
Christian	221 (90.6)	23 (9.4)	244
Islam	401 (86.1)	65 (13.9)	466
Shamanism	599 (93.7)	40 (6.3)	639
Others	3 (75.0)	1 (25.0)	4
Total	6874 (93.6)	473 (6.4)	7347

VI. DISCUSSION

There are a lot of factors that influence deciding to become a donor. The legal environment, information on blood necessity, social status, social network are all external factors yet the most important factor in an individual's education level, attitude, and habit.

The main factors influencing blood donation are altruism, empathy, and various social reasons. Regular voluntary non-remunerated donors often donate blood altruistically, but at that, they feel great responsibility to the recipients.[4]

In this survey result we tried to find out the reason for becoming permanent blood donors in Mongolia. The main factors to becoming a blood donor are education level, gender, and attitude of the working environment, and willingness to do good deeds. The result of our survey, the similar trend was defined. 14.6% of blood donors who participated in the survey are permanent blood donors. The majority of blood donors are urban citizens and women, aged 18-35, educated and married.

One unique result of this study was the biggest intention of blood donation among Mongolians is willingness to do the good deed. It could be explained by the traditional Mongolian culture and Buddhism influence. . Liu et al were found that the ethnicity and religion were successfully incorporated into health promotion interventions for ethnic minority groups in a study of health researchers and promoters. Identifying with culture, race/ethnicity, and religious affiliation can influence health behaviors and can promote minority blood donors to benefit the health of others[5].

Oswalt's[6] and Bettinghause et al's[7] reviews were stated on motivation and recruitment of donors and non-donors reported that main motivation of blood donation is an altruism which was defined as "prosocial behavior that has no obvious benefit for the respondent but is beneficial to the recipient".[8]

Another intention of blood donation is the working environment of people which leads to the first blood donation. Not many researchers have found such results. Maybe it relates with the organization's culture of Mongolian institutions.

The research result of Lee et al (2008) shows that only 6% of the first-time donors become regular

[4] Kasraian, L., 2010. Causes of discontinuity of blood donation among donors in Shiraz, Iran: cross-sectional study. Sao Paulo Med J, 128(5): 272-275.

[5] Liu, J. J., Davidson, E., Bhopal, R., White, M., Johnson, M., Netto, G., & Sheikh, A. (2016). Adapting health promotion interventions for ethnic minority groups: A qualitative study. Health Promotion International, 31, 325–334.

[6] Oswalt RM: A review of blood donor motivation and recruit-ment. Transfusion 17:123-135, 1977

[7] Bettinghaus EP, Milkovich MB: Donors and non-donors. Communication and information. Transfusion 15:165-169, 1975

[8] Zillmer EA, Glidden RA, Honaker LM, et al: Mood states in the volunteer blood donor. Transfusion 29:27-30, 1989

donors, and 62% never come again for another donation[9].

The glorification of blood donors contributes to the recruitment of new donors and a positive impact on the distribution of information, and to support regular donors who have voluntarily donated their blood. This result was identical with results of Karen et al (2008)[10], Polonsky, Brijnath, & Renzaho, (2011)[11]; Renzaho & Polonsky, (2013)[12] ; Robbins et al., (2015)[13]; and Tran et al., (2013).[14]

Barriers of blood donation of defined in numbers of studies [15, 16, 17, 18, 19] . According to the Alsalmi et al (2019)[20] The most common reported barrier from blood donation by donors was various fears from donation (67; 16%), in contrast to health reasons (85; 47.2%) according to nondonors. Around 286 (47.8%) students expressed that appreciation certificates are the best motivations for them to donate blood, while 226 (37.8%) preferred academic support such as bonus marks in the courses they take.

Piliavin[21] classified return donors into 2 categories: (1) those who had given 1 to 3 times and those who had donated 4 or more times. Facilitating the transition of repeat donors to the latter classification was found to be critical in generating long-term repeat donors. The result of our survey shows that half of the people who had donated blood were in the first category.

In conclusion, the majority of respondents believed that they did not give blood for their

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blood because they will have low blood volume or didn't know where to donate their blood or either because of illnesses. The main reason for the rejection of blood donation is the stereotypical "male blood doesn't reproduce". Other reasons are: Family doesn't allow; risk of infection and busy schedule. Also, respondents failed to donate their blood because family is not allowed, afraid, risk of infection, doesn't want to and busy. The main factors to becoming a blood donor are education level, gender, attitude of working environment, and willingness to do good deeds. Thus, actions should be done to encouraging donors to continuing donation could have an important influence on maintaining the overall donor pool.

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Malaria Parasite Detection Among Students Attending Babcock University: Microscopy Versus Malaria Rapid Diagnostic and Urine Malaria Tests

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ABSTRACT

Introduction: Malaria is a mosquito borne blood disease with a worldwide distribution transmitted through blood meals of infected female anopheles mosquitoes (World Health Organization (WHO, 2018). Malaria parasites is usually confirmed and assessed by microscopic examination of blood films or by malaria Rapid Diagnostic Tests (mRDT) which may include Histidine-Rich Protein 2(HRP2), Plasmodium lactate dehydrogenase (pLDH), Urine Malaria Test (UMT). The microscopic detection of malaria parasite is generally considered as the gold standard in malaria diagnosis due to good sensitivity and specificity. The objective of this study is to assess the performance of malaria Rapid Diagnostic Tests (Histidine rich protein 2 and urine malaria test) with microscopy for the detection of malaria parasite among under- graduate students attending Babcock University.

Methodology: A cross sectional study design was used. The study was carried out between October 2018 to February 2019 in Babcock University/ Babcock University Teaching Hospital, Illishan Remo, Ogun state. A total of two hundred (200) undergraduate students of Babcock University were recruited for this study. Rapid diagnostic tests (HRP-2 and UMT) and microscopy were used as the main diagnostic tools for this research along with questionnaire.

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ABSTRACT

Introduction: Malaria is a mosquito borne blood disease with a worldwide distribution transmitted through blood meals of infected female anopheles mosquitoes (World Health Organization (WHO, 2018). Malaria parasites is usually confirmed and assessed by microscopic examination of blood films or by malaria Rapid Diagnostic Tests (mRDT) which may include Histidine-Rich Protein 2(HRP2), *Plasmodium lactate dehydrogenase (pLDH), Urine Malaria Test (UMT). The microscopic detection of malaria parasite is generally considered as the gold standard in malaria diagnosis due to good sensitivity and specificity. The objective of this study is to assess the performance of malaria Rapid Diagnostic Tests (Histidine rich protein 2 and urine malaria test) with microscopy for the detection of malaria parasite among under-graduate students attending Babcock University.*

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Result: the study revealed that 100% of the respondents knew about malaria as a disease. 14% of the study population had been hospitalized this year of which 64.3% were due to malaria and its complications. 0.5% of the study population had malaria less than 1 month , 14.5% had malaria in less than 3 months ago, 24% had malaria within 4-6 months ago and 24.5% didn't know when they last had malaria. Of the proportion of study subjects that visited the hospital (59.5%), microscopy was used in a greater percentage to diagnose (60.5%), none were diagnosed using RDTs, with the rest (39.5%) unsure of the method used for diagnosis. The HRP-2 tested positive for only one (0.5%) patient sample collected whilst, UMT tested negative for all samples (100%). Microscopy, the gold standard tested negative for all patients recruited for the research.

Conclusion: The prevalence of malaria parasite amongst undergraduate student of Babcock University is very low due to good knowledge and awareness of malaria parasites and its prevention. It was also revealed that HRP is a sensitive rapid diagnostic test while, UMT is more specific.

Keywords: urine malaria test, undergraduate students, microscopy, malaria, rapid diagnostic tests.

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I. BACKGROUND OF STUDY

Malaria is a severe mosquito borne blood disease with a worldwide distribution transmitted through blood meals of infected female anopheles mosquitoes (WHO, 2018). It is part of the most common endemic disease worldwide. According to the WHO, there are approximately 200 million cases of malaria in 91 countries and >500,000 deaths each year especially the sub-Saharan Africa (WHO, 2017). Africa countries under WHO carries a disproportionately high share of the global malaria burden because of high level of poverty. In 2016, the African countries had up to 90% of health cases caused by malaria and 92% mortality were caused by malaria. Children under 5years, gravid women and HIV/AIDS patients, together with non-immune travelers, and mobile populations had the highest risk of infection with malaria parasite. (WHO, 2018).

Plasmodium. falciparum, vivax, malariae, ovale, and *knowlesi* are the *Plasmodium species* that results to malaria in humans with *Plasmodium falciparum* being the most prevalent and virulent specie. These malaria parasites are known to have various effect in the human body ranging from minor to severe symptoms such as fever, tiredness, vomiting, and headaches, yellowing of skin, seizures, coma, or death. (Caraballo, 2014). Owing to this varied signs and symptoms, the diagnosis for the confirmation of malaria parasite is important in order to commence adequate treatment for the eradication of this parasites and to prevent unnecessary use and abuse of anti-malaria drugs (Abba *et al.*, 2011; Uguonu *et al.*, 2014; Oyibo *et al.,* 2017; Okangba, 2019).

Malaria parasites is usually verified and assessed by examination of blood films using microscopy or malaria Rapid Diagnostic Tests (mRDT) that may include Histidine Rich Protein-2 (HRP2), Plasmodium Lactate Dehydrogenase (pLDH) (Azikiwe *et al.*, 2012; Oyeyemi *et al.,* 2015). The detection of malaria parasite using microscopy is broadly considered as the gold standard diagnosis of malaria because of its good sensitivity and specificity,allows species and stage differentiation, provide accurate parasite qualification, provide lower cost diagnosis when the case load is high and allows reliable monitoring of the response to therapy (Moody, 2002; Tamiru *et al.,* 2015 Okangba *et al.,* 2016). However, microscopy service in remote areas is restricted due the following factors: capital, lack of electric supply, requires equipment not always available or maintainable in remote areas, time consuming, labor–intensive and lack of experienced microscopist (Moody, 2002; Murray *et al.,* 2008; Okangba *et al.,* 2016; Okangba, 2019).

Rapid diagnosis is an important integral effort in reducing morbidity, mortality and incidence of misdiagnosis in the detection of malaria parasite in a malaria suspected patient. The use of MRDTs are currently existing, accurate and quality assured MRDTs are an alternative to the diagnosis of malaria particularly where good quality microscopy services cannot be readily provided (Wongsrichanalai *et al.*, 2007; Okangba *et al.*, 2016). MRDTs are fast, easy to interpret, requires no capital investment or electricity, requires no specific equipment, comparatively easy procedures and provides fast results for making treatment decision and sensitive to clinically significant malaria (Bisoffi *et al.,* 2010; Oyibo *et al.*, 2017).

Malaria Rapid Diagnostic Tests are lateral flow immune-chromatographic antigen-detection test, which is based on the dye-labelled antibodies capture to produce a band visible on a nitrocellulose strip, often covered in plastic housing, known as cassettes. (Moody, 2002; Murray et al., 2008; WHO, 2018). The HRP-2 and *Plasmodium* specific lactate dehydrogenase (Pf-pLDH) is specific for antigens of *Plasmodium falciparum*, antigens of *Plasmodium vivax* is specific *to Plasmodium vivax*-specific Parasite Lactate

Dehydrogenase (Pv-pLDH) and pan-specie Parasite Lactate Dehydrogenase (pan-pLDH) and aldolase is specific for antigens of all *Plasmodium species* (Bell *et al.,* 2006; Nana *et al.,* 2008). Urine malaria test which is also an mRDT for the malaria parasite detection utilizes recombinant monoclonal antibody to detect *Plasmodium falciparum* specific HRP2, a poly-histidine protein, or fragment present in the urine of febrile patient. (Oguonu *et al.,* 2014; Godwin *et al.*, 2018). The usefulness and functioning of mRDTs in management of malaria lies on the efficiency of the diagnosis provided, and they can generate invalid or false results cause by producer errors, storage, transport, operator error, antigenic polymorphism, genetic diversity. (Baker *et al.*, 2005; Tavrow *et al.*, 2007; Real, 2016).

Histidine Rich Protein 2 have been found in several body fluids such as urine, saliva and blood (Rodriguez-del Valle *et al.*, 1999). Base on this discovering, the need to use urine to develop a diagnostic tool for malaria diagnosis was invented and put into existences (Uguonu *et al.,* 2014). Since, blood samples could be harmful or pathogenic when exposed (Nwakanma *et al.,* 2009). There is also the difficulties experienced while trying to collect blood from patients, issue of cultural taboo and procedural difficulties (Uguonu *et al.,* 2014). There is a great prospects in the use of urine as a test matrix, less risk and ease of access to the sample (Oguonu *et al.*, 2014). The blood RDTs have been evaluated using urine without getting a satisfactory result (Genton *et al.,* 1998; Nwakannma *et al.*, 2009). This unsatisfactory results may be due to the degradation of urine excreted protein (Ehrich and Hortsmann, 1985; Mharakurwa *et al.*, 2008). Hence the development of a specific kit that can detect specific malaria antibodies in the urine (Oguonu *et al.*, 2014). The urine based malaria test kit is a recombinant monoclonal antibody based test that detects *P. falciparum* specific HRP2, a poly-histidine protein, or fragment present in the urine of a febrile individual. Access the diagnostic accuracy of the UMT in malaria diagnosis in comparison with benchmarked gold standard blood smear microscopy (Oguonu *et al.*, 2014).

The aim of the research is ascertain the prevalence of malaria, establish the efficacy and functionality of malaria Rapid Diagnostic Tests (PfHRP2 and urine malaria test) and compare the performance of HRP2 and Urine Malaria tests with microscopy for assessment of malaria parasites detection among symptomatic and asymptomatic students attending Babcock University.

II. STATEMENT OF THE PROBLEM

Malaria is the foremost prevalent tropical transmittable disease in the world. The need for accurate, efficient and quick diagnosis of malaria for quick treatment is necessary. Malaria being the most common cause of hospitalization in Babcock University has to be quickly diagnosed for the adequate treatment to be given. This project topic was thus brought forth to discover the efficiency and efficacy of two rapid diagnostic tests compared to the diagnostic gold standard and to discover the prevalence of malaria among undergraduate students of Babcock University.

III. SIGNIFICANCE OF THE STUDY

Malaria is the highest cause of student hospitalization in Babcock University, therefore the need for efficient and quick diagnosis with the use of clinical investigations is necessary. This study would help to estimate the widespread of malaria and the best investigation(s) for the detection of malaria parasites among Babcock University students.

IV. MATERIALS AND METHODS

4.1 Study Site

The field study was conducted at Babcock University Teaching Hospital, Ilishan-Remo, Ogun state, Nigeria. Laboratory studies were conducted in the Department of Medical Microbiology and Parasitology, Benjamin Carson (SNR.) School of Medicine, College of Health and Medical Sciences Babcock University. In this study the first 100 subjects recruited into the

study, microscopy was compared against mRDT (PfHRP-2), and in the last 100 subjects recruited, microscopy was compared against mRDT (UMT and PfHRP-2). This is because of the limited amount of Urine Malaria Test kits supplied.

4.2 Study Design and Sample size Determination

The study was a cross sectional study. A sample size of 200 individuals was calculated using a standard formula.

$$N = \frac{(1.96 + 1.28)^2 \times P(1-P)}{(P - P_0)^2 / P_x}$$

with a malaria prevalence (P_x) of 48%, an estimated sensitivity (P) of 85% for SD Bioline RDT specific for HRP-2, and WHO-recommended minimum sensitivity (P_o) of ≥ 95% at ≥ 100 parasites/µL and a 5% precision (Olufemi, *et al.*, 2015)

4.3 Inclusion and exclusion criteria

Inclusion criteria includes individuals who were not on antimalarial in the last two weeks and gave consent. While exclusion criteria includes individuals who didn't give consent and on treatment for malaria.

4.4 Blood Sample Collection and Blood film Preparation

Blood samples were collected from participants that met all the inclusion criteria. The blood was collected by venipuncture and at least 3mls of blood was collected into EDTA bottles. The EDTA bottles were mixed thoroughly by gentle inversion of the bottles. Each bottle was labeled with the patient number and date of blood collection (DD/MM/YY), using a marker pen. The blood sample was used to prepare smears.

4.5 Thin and thick films Preparation

Two slides per patient were used to prepare the thin and thick films and were labeled using lead pencils to write the individual's number and date at the tail end of the slide (Samina *et al.,* 2017). For the thin film, 2µL of blood was dropped near the frosted end of a grease free clean slide using an automated micropipette. Another "spreader" slide was held with polished edges at a 40-45° angle and then drawn into the 2µL of blood. The blood was allowed to spread almost to the width of the slide. The "spreader" slide was then rapidly and smoothly pushed to the opposite end of the slides. The smear was allowed to dry at room temperature. The smears prepared must have feathered edges. The thin smears were fixed by dipping them in absolute methanol. (Norgan *et al.,* 2013*)*. Thick smears were prepared with 12µL of blood with a diameter of 12mm template. The corner of another slide was used to spread the blood using a circular motion until it was the size of a dime. The smear was allowed to dry thoroughly in a flat level position at room temperature for 8 to 12hours. The films were stained with 10% Giemsa stain for 10 minutes and washed with buffer water (Oyetunde *et al.,* 2015). The slides were viewed under the microscope using x100 magnification (oil immersion objective) for malaria parasites detection (Olufemi *et al.*, 2015).

V. DETERMINING PARASITAEMIA

With two tally counters were used, one was used for asexual stage of the parasite and the other for white blood cells (WBC) count. Individual parasite densities were determined by counting the number of asexual parasites against 500WBCs in a thick film which was positive, and parasite counts were computed and reported in parasites/µL blood using the standard 8,000WBCs (Olasehinde *et al.,* 2010; WHO, 2010). A blood slide examination of 200 high-power fields which did not show the presence of asexual forms of *Plasmodium species* was considered negative. (Olufemi *et al.,* 2015).

5.1 Histidine Rich Protein-2 and Urine Malaria Test Procedure

Each mRDT pack was observed for expiration, its desiccant was examined for color change, and the

validity of each test result was ensured by the presence of a control line. Manufacturer's instructions and standardized mRDT job aid were used to conduct the test. Used mRDT cassettes, blood transfer devices, and other non-sharp wastes were discarded in a waste bin, and lancets in sharps container.

Urine malaria test is based on the fact that there are elevated level of specific protein or protein fragment in a patients with clinical malaria which reacts cognate recombinant monoclonal antibody reagents were developed. The tests is quantitative and it consists of nitrocellulose membrane strip which has relevant antibody reagent and controls which are immobilized at the membrane of specific individual site. When the immunochromatographic dipstick is dipped in urine, specific malaria parasite protein present in the urine migrate and interacts with immobilized cognate monoclonal antibody resulting in dark-colored strips on the dipstick. The UMT strips were individually packaged in a sealed Mylar foil pouch with a desiccant, and stored at room temperature for the entire period of the study. (Moll *et al.*, 2008; Uguonu *et al.,* 2014). To perform the urine test, the UMT strip was dipped in 5ml of urine for two minutes to allow the sample to wick and saturate the strip. The strip was then removed, placed on its foil pouch packaging and incubated for 20 minutes. The results was then reported as negative, positive, or un-interpretable: if two visible lines appear on the strip (even if very faint) the test is positive; if only the control line appears, the test was positive. Tests results were reported as un-interpretable, i.e., failure to observe a control line or the presence of a darkly stained background that obscured the test lines, was repeated to resolve the discrepant event. (Moll *et al.*, 2008)

5.2 Questionnaire and Data Analysis

A study team trained on the use of questionnaire and collection of blood and urine samples were assigned to this study. Standardized structured and pretested questionnaire coupled with an informed consent form were given to individuals within the eligibility criteria for the research. Data generated from this study was entered into EPI-INFO version 6.04. The results gotten from the questionnaires and laboratory were analysed using a Statistical Package for Social Sciences (SPSS) version 22.0.

5.3 Ethical Approval

Approval was gotten to conduct this study from Ethics and Research Committee, Benjamin Carson (SNR.) School of Medicine, Babcock University, Ilishan-Remo, Ogun state with the reference number, BUHREC583/18. Informed consent were given to the individuals on the purpose of the study. They were also informed of their right to withdraw from the study. The entire study was conducted in line with Good clinical laboratory practice and Good clinical practice.

VI. RESULT

The respondents of the study were undergraduate students of Babcock University. A total sample size of 200 students were enrolled for this study. The results gotten were presented using tables and charts showing the variables, number of participant and the corresponding percentage of participant in separate columns.

Table 1: shows the demographic data of the participants, including their age, sex, religion, and ethnicity, and marital status, level of education, department, level and contact address. The age group of 20-24 had the highest percentage of proportion of 93.5% followed by 15-19 (5.0%). The lowest group was 25-29 (0.5%0) with no participant above the age of 34 years. 50.5% were males and the rest were females. From the analysis, participants of this study were from different ethnic group. Of which majority were Yoruba's (46.5%), followed by the Igbos (43.0%), Hausa (5.0%), Urhobo (2.5%) and an international student who participated in the study, a Ghanaian having 0.5% of the total participants.

Participants were of different departments of various schools in the university. They include accounting, anatomy, biochemistry, business administration, computer science, economics, history, information and resource management, language and literary studies, mass communication, medical laboratory science, nursing, nutrition and dietetics, political science, religious studies and medicine and surgery (which carry majority participants). From the analysis all the undergraduate levels participated in the study with each level having its own percentage. It was observed that 500level student were the major participant of the study having 28.5%, followed by 200 level (24.0%), 100 level (23.5%), 300 level (12.0%), 400 level (11.0%) and the least which was 600 level having 1% of the total participant.

Table 1: Sociodemographic data

VARIABLE		N (200)	Percentage (%)
AGE	15-19	10	5.0
	20-24	187	93.5
	25-29	1	0.5
	30-34	2	1.0
	Above 34	0	0.0
SEX	Male	101	50.5
	Female	99	49.5
TRIBE	Yoruba	93	46.5
	Igbo	86	43.0
	Hausa	10	5.0
	Edo	5	2.5
	Ghana	1	0.5
	Urhobo	5	2.5
EDUCATIONAL LEVEL	Primary education	0	0.0
	Secondary education	0	0.0
	Tertiary education	200	100.0
LEVEL	100	47	23.5
	200	48	24.0
	300	24	12.0
	400	22	11.0
	500	57	28.5
	600	2	1.0

Table 2: shows the level of awareness of the undergraduates of Babcock University to malaria. Out of the study population of 200 participants, all the participants (100%) had knowledge of malaria.

Table 2: Knowledge and awareness of malaria among students

	Responds	N=200	Percentage(%)
HEARD OF MALARIA	Yes	200	100.0
	No	0	0.0
	I don't know	0	0.0

Table 3 and Figure 1: shows occurrence and severity of malaria symptoms in undergraduates of Babcock University. Majority of the participants (86%) had not been hospitalized this year, 14% of the participants had been hospitalized this year, 42.9% just once, 42.9% twice, then 14.2% three times. Majority of the population were hospitalized because of malaria or malaria complications (64.3%). The rest were hospitalized for non-malaria causes (25.0%) and unknown causes (10.7%).

Table 3: Occurrence and severity of malaria.

	Number participants (N=28)	Number of times	Percentage (%)
Hospitalized participants	12	1	42.9
	12	2	42.9
	4	3	14.2

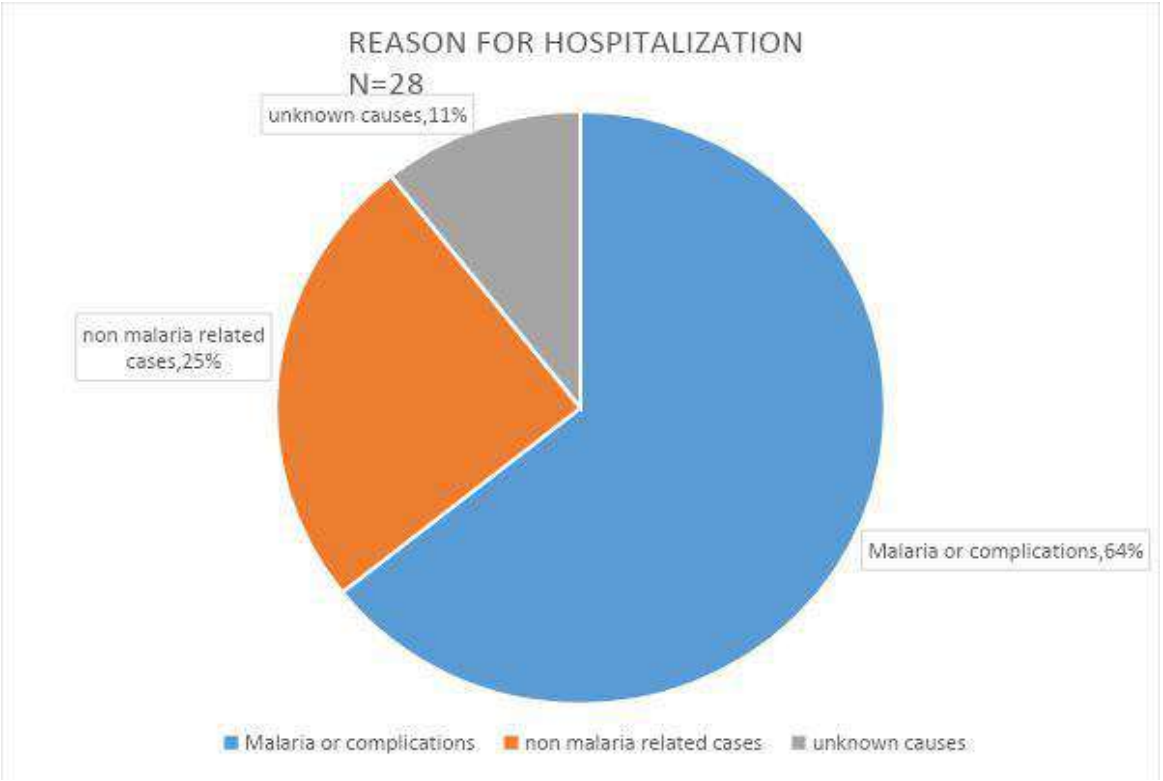

Figure 1: Reasons for hospitalization

Table 4: shows the level of awareness and occurrence of malaria symptoms in Babcock undergraduates as majority visited the health care facility. 36.5% of the study population had a previous history of malaria of > 9 months, 24.0% -within 4-6 months, 14.5% within 1-3 months, 0.5% had a previous history of < 1month, the rest of the study population (24.5%) were unaware of their last malaria manifestation. Majority of the study population visited a health care facility during their last illness (64.5%) and 35.5% did not visit any health care facility.

Table 4: Level of Awareness and Occurrence of Malaria symptoms

		N=200	Percentage (%)
LAST TIME HAD MALARIA	<1 month	1	0.5
	1-3 months	29	14.5
	4-6 months	48	24.0
	>9 months	73	36.5
	I don't know	49	24.5
VISITED ANY HEALTH CARE DURING LAST ILLNESS	Yes	129	64.5
	No	71	35.5

Figure 2: shows the diagnostic methods used for the study, 59.5% of those diagnosed before treatment, 60.5% used microscopy. Non-used RDT (UMT and HRP-2) and 39.5% didn't know the method used for diagnosis. This shows that microscopy is still considered the goal standard for diagnosis of malaria.

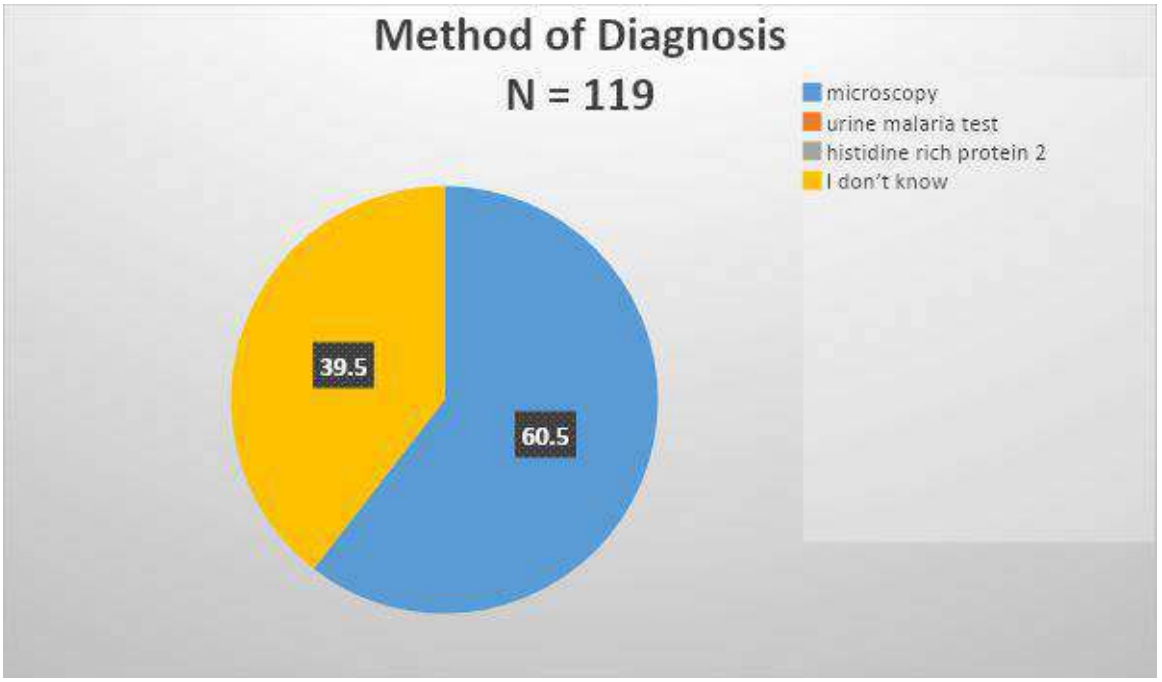

Figure 2: Diagnostic Methods

Figure 3: shows the various antimalarial used in the treatment of malaria. The most used drug for treatment of malaria was Lonart (42%) followed by Arthemether (24.0%) with artemisinin, Lokmal, Macalum, P-Alaxin each being 0.5%. 5.5% of those treated didn't know their drug of treatment. 11.5% didn't get better after treatment.

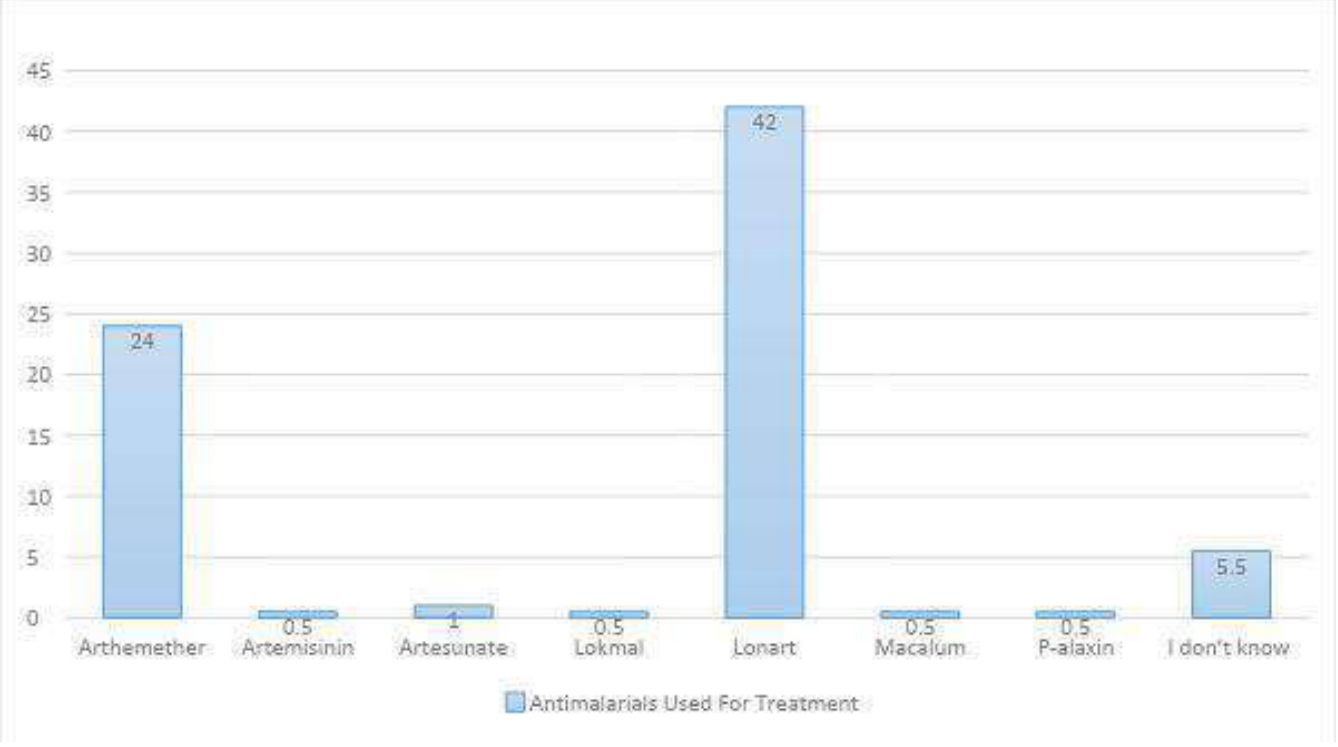

Figure 3: Antimalarials Used For Treatment

Table 5 and Figure 4: reveals the knowledge of participants on preventive measures of malaria infection. A total of 51.5% of participants enrolled for this research, used any of these mosquito-preventive measures. 40% used mosquito bed nets of which 6.8% were treated mosquito nets and 15% LLIN. 77% used insecticides, 22.3% used mosquito repellants and mosquito coils 0.0%.

Table 5: Malaria Infection Preventive Measures

ANY MOSQUITO PREVENTIVE MEASURES	Yes	103	51.5
	No	97	48.5
		N=103	Percentage (%)
IF YES, WHICH ONE	Insecticides	80	77.7
	Mosquito repellants	23	22.3
	Mosquito coil	0	0.0
	Others	0	0.0

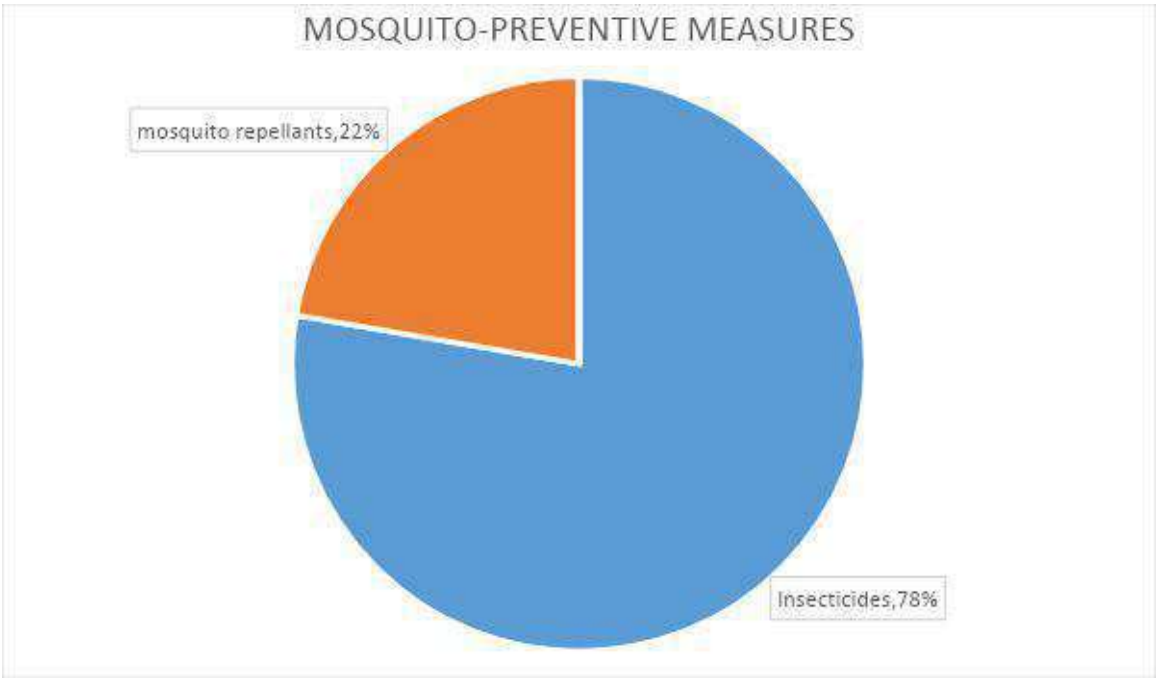

Figure 4: Mosquito Preventive Measures

Table 6: Shows The Result Of The Malaria Diagnostic Methods

DIAGNOSTIC TECHNIQUES	POSITIVITY (%)	NEGATIVITY (%)	TOTAL (%)
MICROSCOPY	0	100	100
UMT	0	100	100
MRDTs	0.5	99.5	100

VII. DISCUSSION

This study is designed to determine the prevalence of malaria parasite among undergraduates of Babcock University and to determine the efficacy and effectiveness of rapid diagnostic test (PfHRP 2 and UMT) using microscopy as the gold standard (Bisoffi *et al.*, 2010; Sani *et al.*, 2013). From the study carried out, the undergraduate students of Babcock University have a good knowledge of malaria and malaria preventive measures like the use of mosquito treated nets (even long lasting mosquito treated nets), mosquito repellants. The prevalence of malaria amongst Babcock undergraduates was absolutely low (0.5%) for RDT, and none of the samples were positive when smeared and evaluated under the microscope. This may have been due to the fact that all the participants (100%) were fully aware of malaria, also had a good knowledge on how to prevent malaria and malaria treatment mostly used by participants were Artemisin Combination Therapy (ACT). With regards to the use of mosquito nets, majority (40%) of the population were aware and utilised mosquito bed nets, which is the same with the study by Nwoke *et al.* (2014) in rural communities in Imo state, it was at 39.2%, and the study by *Ajayi et al* (2014) it was second highest at 17.7% (Ajayi *et al.,* 2014; Nwoke *et al.,* 2014).

The hospitalization this year due to malaria was high (64.3%) this is unusual considering the fact that none of the samples tested positive using microscopy and this can be attributed to the fact that majority of the sample population (64.5%) visited a health care facility during their last days of illness and 76% used antimalarial of which ACT'S (majority used Lonart (42%), Arthemeter (24%), Artesunate (1%), Artemisinin (0.5%), Lokmal (0.5%), Macalum 0.5%), P-alaxin (0.5%) and that would have cleared the parasite in the peripheral blood. In addition, majority of the study population had a previous history of malaria of > 9months (36.5%) and that might also account for the absence of parasite in peripheral blood since subject may not be infected, 24% within 4-6 months, 14.5% within 1-3 months and 0.5% had a previous history of < 1 month, this implies that only a small percent of study population had a recent malarial parasite infection and this is supported by results gotten from microscopy. Also, in other studies (Mahende *et al.*, 2016), false negative results could be obtained on low transmission periods. As transmission declines, condition of submicroscopic infection in both symptomatic and asymptomatic is more likely to rise. This research was carried out during low transmission periods, in the months of January and February. Malaria burden decreases during the dry seasons in Nigeria. The risk of malaria transmission, expressed in terms of sporozoites rates of the parasite and insect inoculation rates, were significantly low during dry season (Olayemi *et al.,* 2018).

Of all participant, 59.5% were diagnosed before treatment when symptoms of malaria began. Of which microscopy was the major diagnostic tool used in detecting the presence of the disease. It was observed that rapid diagnostic tests were not used for the diagnosis of malaria as it recorded 0% of the total percentage. The percentage positive for malaria using PfHRP2(1%) was

unusual because microscopy which is the gold standard tested negative for all participant but possible because the rapid diagnostic test, PfHRP2 only detects antigen of the malaria parasite (Plasmodium falciparum) which could be dead or alive. Therefore, participant who had malaria few days to less than two month and were adequately treated before their samples were collected could test positive for PfHRP2 because of the high sensitivity of PfHRP2. This correlates with the research carried out by Olayemi *et al.*, 2018. (Olayemi *et al.*, 2018). It was also observed that UMT tested negative for all participant which makes a good rapid diagnostic test because the same result was gotten from microscopy which detect the presence of the malaria parasite in the blood and it is therefore safe to say urine malaria test has a good specificity which correlates with a research done by Oguonu *et al.* in 2014, (Oguonu *et al.,* 2014; Godwin *et al.*, 2018).

VIII. CONCLUSION

The study has revealed that the prevalence of malaria among Babcock university undergraduates is very low as they have good knowledge and awareness about malaria parasite and prevention which includes use of long lasting mosquito treated net, use of mosquito repellants, insecticides, mosquito coil and others and could seek medical attention once symptoms of malaria arose, complying with the drugs prescribed by the medical personnel. It was also revealed that the rapid diagnostic test for the detection of malaria parasite Histidine Rich Protein-2 was more sensitive while the Urine Malaria Test (UMT) showed more specificity because HRP-2 could detect presence of parasite in the peripheral blood whether dead or alive using the antigens while UMT which is specific determines the absence of a disease in an individual.

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Conflict of Interest:

The authors declare that they have no conflicts of interest.

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The Effect of Initial Fluorodeoxyglucose Uptake in the Liver and Spleen on Treatment Success and Prognosis Running Head: Initial Fdg Uptake in Liver and Spleen

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ABSTRACT

Introduction: Diffuse large B cell lymphoma (DLBCL) is the most common and aggressive form of Non-Hodgkin Lymphomas. For many years, monoclonal antibody and multiple drug combination chemotherapies have been preferred in its treatment. In addition to the classifications such as International Prognostic Index (IPI), Revised International Prognostic Index (R-IPI) or The National Comprehensive Cancer Network- International Prognostic Index (NCCN-IPI) which predict prognosis and survival in DLBCL patients, many studies are conducted to find easier, cheaper, faster, applicable prognostic data. We aim to determine the relationship between the fluorodeoxyglucose (FDG) uptake in the liver and spleen and prognosis, treatment response, relapse and survival in patients with DLBCL.

Material and Method: Patients followed up between 2009-2019 were analyzed retrospectively. Age, gender, laboratory, PET / CT liver-spleen SUVmax, Ann Arbor stage, ECOG scale, presence of extranodal involvement, presence of B symptoms, IPI score, treatment responses, follow-up period, recurrence and overall survival were recorded.

Results: The median SUVmax of the liver was 3.87 (range: 2.04-19.70) and the median SUVmax of the spleen was 3.1 (range: 1.75-58.85). Based on the median figures of SUVmax, the patients were divided into two groups. The IPI score distribution between the low-high SUVmax groups did not differ significantly ($p > 0.05$) in terms of treatment response, recurrence and overall survival.

Keywords: diffuse large b cell lymphoma (dlbcl), pet / ct, suvmax fluorodeoxyglucose (fdg), prog- nostic factor.

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Discussion: There is no study on initial liver and spleen SUVmax in the literature. In studies with the highest median tumor or total body SUVmax in DLBCL, as SUVmax increased; decreased progression-free survival, decreased treatment response, increased recurrence and poor prognosis were detected. In our study, there was no significant difference between liver and spleen SUVmax groups in terms of age, gender, clinical symptoms, IPI prognosis score, treatment response, recurrence and survival.

Keywords: diffuse large b cell lymphoma (dlbcl), pet / ct, suvmax fluorodeoxyglucose (fdg), prognostic factor.

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I. INTRODUCTION

Non-Hodgkin Lymphoma (NHL) ranks first among all hematological malignancies, although lymphomas accounts for only 3% of all cancers. DLBCL is a heterogeneous group of tumors consisting of large and transformed B cells (1). Its incidence increases with age; the median age of diagnosis is 64. It is more common in men and 55% of patients are male (2, 3). It may appear as de novo or may be histologically transformed from indolent lymphomas. The disease typically occurs as a fast-growing nodal or extranodal mass associated with systemic symptoms (4).

Clinical and demographic parameters such as age, gender, presence of B symptoms, areas of nodal and extranodal involvement, clinical stage and

serum lactate dehydrogenase (LDH) level have frequently been the subject of research in diffuse large B cell lymphomas. While these variables may affect survival independently of each other, the first most frequently used in predicting the prognosis calculated by evaluating a few parameters was defined after the first described in 1993. It is the "International Prognostic Index (IPI)" (5-7). Clinically, IPI or Revised IPI (R-IPI) scoring system is used to determine prognosis. These clinical parameters and IPI score are not always sufficient to determine the prognosis (8).

Instead of using fluoride-18 fluorodeoxyglucose positron emission tomography (F18-FDG PET) or computed tomography (CT) alone, the most useful method is FDG PET / CT (9-11). As an interim evaluation or at the end of treatment procedure to determine the final response ; FDG-PET / CT was found to be more sensitive than other conventional imaging methods due to its metabolic nature in revealing active tumor foci in residual masses after treatment and in predicting tumor's biological aggressiveness and prognosis (12).

We aim to determine the relationship between the FDG uptake in the liver and spleen and prognosis, treatment response, relapse and survival in patients with DLBCL. Initial liver and spleen FDG uptake SUVmax, as a new prognostic indicator, it was intended to be used as an early marker for the treatment resistance, relapse and survival.

II. MATERIAL AND METHOD

Patients followed up in our hematology clinic between 01.01.2009 - 01.01.2019 were retrospectively analysed. The data of 77 patients included in the study were obtained from the hospital electronic information management system and by scanning patient files.

Liver and spleen SUVmax on PET/CT, IPI scores of patients, gender and similar demographic data, leukocyte and neutrophil level at the time of diagnosis, presence of B symptoms were recorded. The treatment responses of the patients after 4 cycles of chemotherapy were examined with PET / CT and their responses were recorded according to the Lugano revised response criteria.

Statistical analysis: Average, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured by the Kolmogorov-Smirnov test. Independent sample t test or Mann-Whitney U test was used in the analysis of quantitative independent data. In the analysis of qualitative independent data, chi-squared test, Fischer test was used when chi-squared test conditions were not met. Kaplan-Meier Logrank test was used in survival analysis. SPSS 22.0 program was used to analyse data. Ethics committee approval: Our study was approved by the Clinical Research Ethics Committee of our hospital on 26.04.2019 with the decision number 1810.

III. RESULTS

Seventy-seven (77) patients were analysed, 61% of whom was male and 39% was female. Male / female ratio was calculated as 1.56. Median incidence of age was 55 (range: 18-82). The presence of B symptoms was found to be 36.4%. According to the ECOG performance scale, 16.9% of patients were found to be at stage 2-4. According to the Ann Arbor staging system, 61% of the patients were found to be in advanced stages at the time of diagnosis. Extranodal involvement was observed in 55.8% of patients. According to the IPI score, 27% of patients were found in the risk group with low, 17% low-intermediate, 23% high-intermediate, and 10% high.

The median SUVmax was 3.87 (range: 2.04-19.70) for the liver and 3.1 (range: 1.75-58.85) for the spleen. After 4 cycles of R-CHOP treatment, 55.8% of patients had complete response, 36.4% partial response and 7.8% progression. Recurrence was observed in 5.2% of the patients after a response. During long-term follow-up, 22.1% of patients were found to be exitus. (Table 1.)

Patients were divided into two groups with liver median SUVmax: 3.87. The group with a median value of 3.87 and below and the group with a value higher than 3.87. Ages and genders of the patients did not differ significantly ($p > 0.05$) in

both groups. In the group with high liver SUVmax, the leukocyte and neutrophil values were significantly lower ($p < 0.05$) than the group with low SUVmax group. Among the liver SUVmax groups there was no significant difference ($p > 0.05$) in ECOG distribution and IPI, extranodal involvement, B symptom presence, treatment responses, recurrence, overall survival and mortality. (Tables 2 and 4)

When the relationship between low and high spleen SUVmax groups was examined, the group with a SUVmax of 3.1 and below is considered to be the group with low SUVmax and those with a value of higher than 3.1 are considered as the group with high SUVmax. The age and gender distribution of the patients did not differ significantly ($p > 0.05$) in the group with low spleen SUVmax and high spleen SUVmax. In addition, there was no significant difference ($p > 0.05$) between the two groups in terms of ECOG distribution, IPI score, presence of B symptoms, treatment responses, relapse, survival and mortality. (Tables 3 and 4)

IV. DISCUSSION

Diffuse large B cell lymphoma is the most common aggressive form of NHL (14). DLBCL is a highly heterogeneous disease and 30-40% of patients show progression and recurrence despite standard chemo-immunotherapy (15). Therefore, defining prognostic factors that can be easily and accurately classified into appropriate risk groups of patients with DLBCL is very important for disease management.

Although PET / CT staging is used widely in patients with DLBCL to evaluate early treatment response and to evaluate residual lesions with high sensitivity at the end of treatment, studies on SUVmax are very few (16-18). Based on the widespread usage of PET / CT in the management of DLBCL and with increasing evidence of the prognostic value of PET / CT parameters, SUVmax is the most studied parameter, partly due to its convenience and high repeatability (19).

In the literature, there are studies on SUVmax ratios in patients with hematological and solid organ malignancies, especially with DLBCL, but there is no study on liver and spleen SUVmax. Our study is the first in the literature in this context. In several studies, it has been shown that SUVmax is associated with survival before treatment in non-small cell lung cancer, oesophageal cancer, colorectal cancer and other solid tumors (20-22).

Huang et al. (23), in a retrospective study conducted in 2016, examined the relationship of FDG uptake involvement with clinico-pathological factors and prognosis in 140 new DLBCL patients. There was a significant difference between low and high SUVmax groups in terms of progression-free survival. In addition, Byun et al (24) and Hirose et al (25) found a significant relationship between SUVmax and IPI risk groups in their studies. In a study by Chihara et al. (26) in 2011, 110 new DLBCL patients were retrospectively analyzed; shorter overall survival and progression-free survival were detected, regardless of IPI, in the high SUVmax group. In addition, the high SUVmax was associated with a low complete response. In the retrospective study conducted by Miyazaki et al. (27) in 2012, it was found that the low SUVmax group in 50 newly diagnosed DLBCL patients showed a better prognosis than the high SUVmax group.

In our study, there was no significant difference between low and high liver and spleen SUVmax groups in terms of age, gender, clinical symptoms, IPI prognosis score, treatment response, recurrence and survival. In the literature, there is no study on liver and spleen SUVmax ratios. In studies with the highest median tumor or total body SUVmax in DLBCL, as SUVmax increased, decreased progression-free survival, decreased treatment response, increased recurrence and poor prognosis were detected. (23-27). When all studies were analyzed, it was observed that different values were used for the SUVmax threshold and those were quite high compared to our cut off values. In these studies we mentioned, a significant difference was observed between the low and high SUVmax groups depending on the high cut off values. Our threshold values have the lowest values compared to literature. The use of different threshold values may have affected the results of the study. A multicentre analysis is required to find the appropriate threshold. The

lower leukocyte and neutrophil values found in the group with high liver SUVmax may provide information about bone marrow involvement and may help with cytopenia prediction after chemotherapy; however, it should be said that a more detailed study is needed to support these comments.

In conclusion, our study is the first in the literature to examine the relationship between liver and spleen SUVmax and DLBCL prognosis and treatment. Although no significant difference was found among the disease parameters; we think that prospective studies with larger patient groups may yield different results.

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We respectfully remember all the colleagues we lost in the COVID-19 fight:

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Conflict Of Interest

None to declare.

Informed Consent

An informed consent obtained from all of our patients to publish this study.

Author Contributions

All authors contributed to the editing of the manuscript. IS wrote the manuscript and made tables.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Table 1: Demographic Datas and Patient Characteristics

		Min-Max	Median	Mean.±s.d./n-%
Age		18.00 - 82.00	55.00	55 ± 14.78
Gender	Female			30 39.0%
	Male			47 61.0%
Liver SUVmax		2.04 - 19.70	3.87	4 ± 2.42
Spleen SUVmax		1.75 - 58.85	3.1	6 ± 8.17
Leukocyte		1.01 - 30.91	7.79	9 ± 4.79
Neutrophil		0.24 - 27.99	5.01	7 ± 4.66
Follow Up Period (Month)		5.33 - 97.07	28.88	35 ± 21.78
ECOG	0-1			64 83.1%
	2-4			13 16.9%
Stage	I			4 5.2%
	II			26 33.8%
	III			25 32.5%
	IV			22 28.6%
LDH	(-)			47 61.0%
	(+)			30 39.0%
IPI Score	Low			27 35.1%
	Low-intermediate			17 22.1%
	High			10 13.0%
	High-intermediate			23 29.9%
Presence of B Sypmtoms	(-)			49 63.6%
	(+)			28 36.4%
Extranodal Involvement	(-)			34 44.2%
	(+)			43 55.8%
Treatment Response	(-)			34 44.2%
	(+)			43 55.8%
	Partial Response			*28 36.4%*
	Progression			*6 7.8%*
	Complete Response			*43 55.8%*
Recurrence	(-)			73 94.8%
	(+)			4 5.2%
Exitus	(-)			60 77.9%
	(+)			17 22.1%

Table 2: Comparison of Liver SUVmax Subgroups

		Liver- High SUVmax Group		Liver- Low SUVmax Group		P
		Mean.±s.d./n-%	Median	Mean.±s.d./n-%	Median	
Age		52.0 ± 16.3	54.0	58.7 ± 12.4	56.5	0.087 [m]
Gender	Female	13 33.3%		17 43.6%		0.305 [X²]
	Male	26 66.7%		21 53.8%		
Liver SUVmax		3.1 ± 0.6	3.3	5.6 ± 2.9	4.4	***0.000*** [m]
Spleen SUVmax		4.0 ± 4.9	2.7	7.4 ± 10.4	3.7	***0.000*** [m]
Leukocyte		10.7 ± 5.6	10.3	7.7 ± 3.9	6.9	***0.002*** [m]
Neutrophil		8.3 ± 5.5	7.7	5.1 ± 3.4	4.3	***0.001*** [m]
Follow Up Period (Month)		36.6 ± 20.6	34.5	33.3 ± 23.2	24.7	0.338 [m]
ECOG	0-1	33 84.6%		31 79.5%		0.702 [X²]
	2-4	6 15.4%		7 17.9%		
Stage	I	3 7.7%		1 2.6%		0.499 [X²]
	II	15 38.5%		11 28.2%		
	III	12 30.8%		13 33.3%		
	IV	9 23.1%		13 33.3%		
LDH	(-)	23 59.0%		24 61.5%		0.707 [X²]
	(+)	16 41.0%		14 35.9%		
IPI Score	Low	15 38.5%		12 30.8%		0.143 [X²]
	Low-intermediate	11 28.2%		6 15.4%		
	High	2 5.1%		8 20.5%		
	High-intermediate	11 28.2%		12 30.8%		
Presence of B Symptoms	(-)	21 53.8%		28 71.8%		0.070 [X²]
	(+)	18 46.2%		10 25.6%		
Extranodal Involvement	(-)	20 51.3%		14 35.9%		0.202 [X²]
	(+)	19 48.7%		24 61.5%		
Treatment Response	(-)	20 51.3%		14 35.9%		0.202 [X²]
	(+)	19 48.7%		24 61.5%		
	Partial Response	*15* *38.5%*		*13* *33.3%*		
	Progression	*5* *12.8%*		*1* *2.6%*		
	Complete Response	*19* *48.7%*		*24* *61.5%*		
Recurrence	(-)	37 94.9%		36 92.3%		0.979 [X²]
	(+)	2 5.1%		2 5.1%		
Exitus	(-)	30 76.9%		30 76.9%		0.830 [X²]
	(+)	9 23.1%		8 20.5%		

[t] t test / [m] Mann-Whitney u test / [X²] Chi-Squared test (Fischer test)

Table 3: Comparison of Spleen SUVmax Subgroups

		Spleen- Low SUVmax Group		Spleen- High SUVmax Group		p	
		Mean.±s.d./n-%	Median	Mean.±s.d./n-%	Median		
Age		52.6 ± 16.1	53.5	57.1 ± 13.5	57.5	0.179	m
Gender	Female	13 33.3%		17 43.6%		0.842	X^2
	Male	21 53.8%		25 64.1%			
Liver SUVmax		3.7 ± 1.5	3.4	4.8 ± 2.9	4.3	***0.001***	m
Spleen SUVmax		2.5 ± 0.4	2.6	8.2 ± 10.3	4.3	***0.000***	m
Leukocyte		10.1 ± 5.6	9.3	8.2 ± 3.8	7.1	0.112	m
Neutrophil		7.5 ± 5.6	6.2	5.9 ± 3.6	4.7	0.210	m
Follow Up Period (Month)		34.9 ± 20.8	34.1	35.5 ± 22.8	25.6	0.950	m
ECOG	0-1	29 74.4%		34 87.2%		0.617	X^2
	2-4	5 12.8%		8 20.5%			
Stage	I	3 7.7%		1 2.6%		0.502	X^2
	II	16 41.0%		10 25.6%			
	III	8 20.5%		17 43.6%			
	IV	7 17.9%		14 35.9%			
LDH	(-)	22 56.4%		24 61.5%		0.184	X^2
	(+)	12 30.8%		18 46.2%			
IPI Score	Low	15 38.5%		12 30.8%		0.066	X^2
	Low-intermediate	9 23.1%		8 20.5%			
	High	2 5.1%		8 20.5%			
	High-intermediate	8 20.5%		14 35.9%			
Presence of B Symptoms	(-)	22 56.4%		26 66.7%		0.801	X^2
	(+)	12 30.8%		16 41.0%			
Extranodal Involvement	(-)	19 48.7%		15 38.5%		0.079	X^2
	(+)	15 38.5%		27 69.2%			
Treatment Response	(-)	17 43.6%		16 41.0%		0.298	X^2
	(+)	17 43.6%		26 66.7%			
	Partial Response	*15*	*38.5%*	*14*	*35.9%*		
	Progression	*2*	*5.1%*	*4*	*10.3%*		
	Compelete Response	*17*	*43,6%*	*26*	*66.7%*		
Recurrence	(-)	32 82.1%		40 %13		0.828	X^2
	(+)	2 5.1%		2 5.1%			
Exitus	(-)	26 66.7%		33 84.6%		0.827	X^2
	(+)	8 20.5%		9 23.1%			

[t] t test / [m] Mann-whitney u test / X^2 Chi-Squared test (Fischer test)

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Table 4: Comparison of Survival in Subgroups

	Predicted Survival (Month)	95% Confidence Interval	p
Liver- Low SUVmax Group	54.30	46.84-61.76	0.991
Liver- High SUVmax Group	75.43	62.30-88.57	
Spleen- Low SUVmax Group	53.56	45.24-61.89	0.838
Spleen- High SUVmax Group	76.03	64.00-88.06	

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Cardiovascular Risk Factors and Cardiovascular Risk in People Living with HIV: Comparison of Four Cardiovascular Risk Prediction Algorithms

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ABSTRACT

Introduction: The objective of our study was to evaluate, in a population of Togolese People Living With HIV (PLWHIV), the agreement between three scores derived from the general population namely the Framingham score, the Systematic Coronary Risk Evaluation (SCORE), the evaluation of the cardiovascular risk (CVR) according to the World Health Organization (WHO) and the CVR evaluation equation derived from the Data collection on Adverse effects of anti-HIV Drugs (D.A.D).

Methods: We conducted a descriptive and analytical cross-sectional study including 212 HIV-infected patients recruited from the day hospital of the Infectious Diseases Department of the Sylvanus Olympio University Hospital. The level of agreement between the different scores was estimated using the Pearson correlation test and the Cohen Kappa coefficient.

Keywords: cardiovascular risk, HIV, framingham, D.A.D, score, togo.

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Results: The median age of the participants (68.9% female) was 50.2 years (IQR: 44.8-56.0). Eighty-seven point seven percent of the participants were on highly active antiretroviral therapy, 87.1% of whom were on a combination of two nucleoside inhibitors and one non-nucleoside inhibitor. The most represented cardiovascular risk factors were abdominal obesity (56.1%), HDL hypocholesterolemia (52.4%) and hypertension (44.8%). The median cardiovascular risk was 6.3% (IQR: 3.9-11.2), 0.0% (IQR: 0.0-1.0), 4.0% (IQR: 3.0-8.0), 3.0% (IQR: 1.95-5.01), based on the Framingham, SCORE, WHO and D.A.D scores respectively. There was a strong positive and statistically significant correlation between CVR scores based on the general population and scores obtained using the D.A.D algorithm: Framingham and D.A.D ($r = 0.80$; $p < 0.001$); SCORE and D.A.D ($r = 0.58$; $p < 0.001$); WHO and D.A.D ($r = 0.65$; $p < 0.001$). The level of agreement in classifying low, moderate and high risk patients between the Framingham score and the D.A.D score was 71.2% ($\kappa = 0.19$ CI: 0.09-0.29; $p < 0.001$). The SCORE risk and the WHO score showed respectively an agreement level of 89.6% ($\kappa = 0.28$ CI: 0.12-0.43; $p < 0.001$) and 83.9% ($\kappa = 0.21$ CI: 0.06-0.35; $p < 0.001$) with the D.A.D score. Conclusion: The overall CVR estimated by the different CVR estimation scores allowed us to highlight a low prevalence of PLWHIV with high CVR. The WHO clinical CVR estimation scale could be a low cost alternative to evaluate CVR in resource-limited countries such as Togo.

Keywords: cardiovascular risk, hiv, framingham, d.a.d , score, togo.

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I. INTRODUCTION

The World Health Organization (WHO) estimates that 17.7 million deaths worldwide are attributable to cardiovascular diseases (CVD), accounting for 31% of total global mortality in 2015[1]. Between 1990 and 2013, Sub-Saharan

Africa recorded an 81% increase in the number of CVD deaths [2]. At the same time, this same region of Africa is facing another scourge, that of HIV/AIDS. Indeed, in 2018, it is estimated that sub-Saharan Africa was home to 2/3 of the 37.9 million people living with HIV (PLWHIV) in the world [3]. Thanks to active screening and increased access to Highly Active Antiretroviral Therapy (HAART), the life expectancy of PLWHIV has been steadily increasing [3,4]. The average age of PLWHIV is increasing but with new challenges such as non-communicable diseases, especially CVD [5,6]. According to published data, the risk of cardiovascular events is twice as high among PLWHIV compared to HIV-negative people [7,8] and this at younger ages [6]. Explanations for this high CVD risk are HIV-related chronic arterial inflammation on the one hand [9,10] and HAART [11] on the other hand, which exposes PLWHIV to dyslipidemia [12,13], lipid distribution disorders [14] and carbohydrate metabolism disorders [14–16] thus increasing their risk of atherosclerosis and metabolic syndrome [17].

According to the recommendations of the WHO, global cardiovascular risk (CVR) evaluation is a prerequisite for the institution of any primary prevention intervention for CVD [18]. Several cardiovascular risk evaluation scales exist as tools for this purpose, the best known of which is the Framingham score but also the Systematic Coronary Risk Evaluation (SCORE) proposed by the European Society of Cardiology [19]. In sub-Saharan Africa, the WHO proposes two CVR evaluation tables; one that takes into account clinical data and cholesterol levels and the other that takes into account only clinical parameters [20].

However, it must be recognized that the three above-mentioned scores were developed from a general population and none of the three takes into account in their CVR estimation, variables specific to HIV infection such as current HAART molecules, CD4 count, viral load, duration of HIV infection, duration of exposure to HAART.

The D.A.D study (Data collection on Adverse effects of anti-HIV Drugs) made it possible to develop an algorithm for calculating the overall CVR and is considered the currently available reference score in terms of cardiovascular risk evaluation specific to PLWHIV [21].

The objective of our work was first to evaluate the overall cardiovascular risk of PLWHIV in Togo according to the Framingham score, SCORE, the WHO scale (dedicated to sub-Saharan African countries based on clinical data only), D.A.D and then compare the three scores based on the general population with the PLWHIV-specific score. The ultimate research question, being to know at the practical level which of the three Framingham, SCORE, WHO, scores could be an alternative tool to the D.A.D to evaluate overall CVR among PLWHIV in resource-constrained settings.

II. METHOD

2.1 Presentation of the study site

The Ambulatory Treatment Center (ATC) of the Infectious Diseases Department of the Sylvanus Olympio University Hospital in Lome (CHU-SO) served as the framework for our study. It is the reference service for the care of PLWHIV in Togo. Approximately three thousand five hundred patients are regularly followed up with HAART.

2.2 Type and period of study

We conducted a cross-sectional descriptive and analytical study on patients under HAART received in consultation for their routine follow-up and newly screened PLWHIV who were initiated on HAART from May 1, 2019 to October 31, 2019, i.e. a period of six months.

2.3 Study population

The inclusion criteria for our study were:

- Any clinically stable PLWHIV on HAART received in follow-up consultation during the study period, aged at least 40 years old regularly followed for at least six months at the ATC of CHU SO, not having missed any follow-up appointment during the six month preceding the day of consultation.

- All PLWHIV naïve to HAART, referred for HAART initiation consultation during the study period.
- To have the results of a blood test no more than three months old consisting of a serum assay of total cholesterol (CT), triglycerides (TG), HDL- cholesterol (HDL-c), LDL-cholesterol (LDL-c), CD4 count and a recent viral load (CV) measurement.

The following were excluded from our study:

- Patients with a personal history of angina, myocardial infarction or stroke.
- Patients on hormonal treatment, on lipid-lowering treatment.
- Patients with thyroid disease.
- Any patient presenting a situation that could lead to an increase in abdominal volume and distort the measurement of waist circumference (pregnant woman, liver pathology with ascites).
- Breastfeeding women.
- Patients who refused to participate in the study.

Patients on HAART were randomly recruited at a rate of 15 patients per week during follow-up visits. All naïve patients who met the inclusion criteria were selected.

III. DATA COLLECTION AND SOURCES

A standardized data collection sheet was designed and used as a support for data collection. Patients were informed in advance of the data collection process. Age, sex, notions of hypertension and diabetes and HIV history, were collected through interviews and the patient's treatment record. Waist circumference was measured with a tape measure wrapped around the waist by the midpoint between the lower edge of the rib and the iliac crest in a plane perpendicular to the major axis of the body. The size was determined without shoes using a measuring rod. The weight was measured using a bathroom scale. Body mass index (BMI) was calculated as the ratio of weight to height squared. A BMI greater than 25kg / m^2 defined overweight. The high waist circumference corresponding to abdominal obesity was defined according to the criteria of the International Diabetes Federation (waist circumference greater than or equal to 94 cm in men and 80 cm in women). Blood pressure was measured for each patient with a mercury manometer twice after 10 minutes of rest. The mean systolic and diastolic figures obtained from both measurements were included in the evaluation of high blood pressure.

Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and / or diastolic blood pressure (DBP) ≥90 mmHg or a known history of hypertension or the use of antihypertensive drugs[22].

The existence of dyslipidemia was defined according to the criteria of the National Cholesterol Education Program, Adult Treatment Panel III which are: total hypercholesterolemia (HCT) if CT ≥ 2.0 g/L, hypertriglyceridemia (HTG) if TG ≥ 1.5 g/L, HDL hypocholesterolemia (HCH) if HDL-c ˂ 0.5 g/L in women and ˂ 0.4 g /L in men, LDL hypercholesterolemia (HCL) if LDL-c ≥ 1.3 g/L.

3.1 Cardiovascular risk evaluation

The cardiovascular risk was estimated for each patient included in the study using four equations to calculate the overall risk of cardiovascular disease (CVD): the Anderson-Framingham CVR score, the Systematic Coronary Risk Evaluation (SCORE), the WHO CVR score dedicated to the western region of Sub-Saharan Africa where Togo is located and the CVD risk equation for PLWHIV derived from the D.A.D cohort.

The Anderson-Framingham equation (FRS) estimates in subjects aged 30 and older the risk of occurrence of CVD at 10 years based on the combination of CVR factors namely age, sex, systolic blood pressure, the use or not of an antihypertensive treatment, the values of the serum total cholesterol level, HDL-c, the existence of active smoking or not, the existence or not of diabetes [23]. Patients are classified into three levels of CVR: low risk (˂10%), moderate (10-20%), high (> 20%).

The European Society of Cardiology's SCORE risk estimates 10-year mortality from cardiovascular event in subjects aged 40 and over and is based on sex, age, systolic blood pressure, whether or not

there is active smoking and total cholesterol level. Patients are classified as low (<3%), moderate (≥ 3% and <5%), high (≥ 5 to <10%) and very high risk (≥ 10%). For our study, high and very high risk patients were grouped into a single "High Risk " group (≥ 5%) to simplify comparisons. With regard to the incidence of coronary heart disease in Togo, we opted for the SCORE table based on the European Society of Cardiology of 2019 recommendations for European countries with low CVR [19].

The WHO CVD risk score for the western region of Sub-Saharan Africa used for our study makes it possible to estimate in subjects aged 40 and over, the 10-year risk of a fatal cardiovascular event (myocardial infarction, cerebrovascular accident, or any other arterial occlusive disease including sudden death by cardiac arrest) taking into account only clinical parameters, namely sex, age, smoking status, body mass index and systolic blood pressure[24]. Given the context of limited resources in this region where Togo is located, we opted for this score because in practice, PLWHIV often have difficulties in honoring on time the unsubsidized biochemical check-ups that they are supposed to honor once a year. According to the WHO score, patients are classified into three levels of cardiovascular risk: low (<10%), moderate (10-20%), high (> 20%) risk.

In order to ensure consistency in the evaluation of CVR, the CVR evaluation according to the D.A.D equation was also evaluated over 10 years. We referred for this purpose to the D.A.D algorithm published by Nina Friis-Møller et al [25]. The equation is based on the combination of age, gender, systolic blood pressure, serum CT and HDL-c level, known or unknown diabetes, active or inactive smoking status, family history of cardiovascular disease, current use of Abacavir, Indinavir or Lopinavir, and number of years spent on Indinavir or Lopinavir. The family history of CVD was defined as the first degree occurence of CVD before age 50 in men and 65 in women [21].

3.2 Statistical analysis of data

All of the data collected was entered into a data entry mask developed in Epi data version 3.1 software and then analyzed using IBM SPSS Statistics 20 statistical software.

Continuous quantitative variables with a normal distribution were expressed as mean and standard deviations if not as medians and interquartile ranges (IQR). Categorical variables were expressed as percentages.

The $\chi 2$ test or Fisher's test was used to compare the proportions. Pearson's correlation test was used to evaluate the degree of correlation between the risk scores obtained according to each algorithm while the agreement between CVD risk evaluation equations was evaluated using Cohen's Kappa coefficient with a 95% confidence interval. A p-value < 0.05 was considered statistically significant. The Kappa coefficient was interpreted as having bad agreement (<0), slight agreement (0–0.20), fair agreement (0.21–0.40), moderate agreement (0.41–0.60), substantial agreement (0.61–0.80) or perfect agreement (0.81-1.00) [26].

3.3 Ethical considerations

The authorization of the head of the Ambulatory Treatment Center for HIV-infected people has been obtained. Informed consent of the patients was obtained. The anonymity and confidentiality of their data were respected.

IV. RESULTS

4.1 General characteristics of the study population

Two hundred and twelve patients were included in our study. Females predominated in a proportion of 68.9% (146) with an M / F sex ratio of 0.45. The median age was 50.2 years (IQR: 44.8-56.0) with a minimum of 40 years and a maximum of 72 years. The 40 to 49.9 age group was the most represented in 48.1%. Almost half of our study population (47.6%) made a living from commerce and were married (48.6%). Eighty-three point five percent (177 patients) of our study population resided in urban areas. The median time since diagnosis of HIV status was 4.1 years (IQR: 2.7-7.2) with a minimum of 1 year and a maximum of 14.4 years. Eight patients (3.8%)

were known to have diabetes and 35 (16.5%) were hypertensive. The notion of active smoking was found in 10 patients, i.e. 4.7%. None of the patients in the sample reported a family history of CVD.

Patients on HAART represented a proportion of 87.7% (186). Their median duration on HAART was 3.6 years (IQR: 2.7-7.3). Among patients on HAART, patients on 1st line made of a combination of two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and one Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) accounted for 87.1% (162) while the remainders were on a combination of two NRTIs and a Protease Inhibitor (PI). With Lamivudine as the common molecule in all combinations, the distribution of patients according by exposure to different ARV molecules was as follows: Tenofovir (90.9%), Abacavir (8.1%), Zidovudine (1.1%), Efavirenz (86.6%), Nevirapine (0.5%), Atazanavir boosted with Ritonavir (12.9%). One hundred and ninety-seven patients or 92.9% of the study population had a recent CD4 count while 83% (176) had a recent viral load measurement. The mean CD4 count was 462 cells / mm^3 (± 252) and the proportion of patients with a CD4 count greater than 500 cells / mm^3 was 41.1% (81 patients). The proportion of patients with suppressed viral load represented 84.1% (148). The remaining characteristics of the study population are presented in Table 1.

Table 1: Socio demographic and HIV infection characteristics of the study population.

Characteristics	Values
Age [Years (IQR)]	50.2 (44.8-56.0)
Age groups in Years n (%)	
40-49.9	102 (48.1)
50-59.9	82 (38.7)
60-69.9	25 (11.8)
≥70	3 (1.4)
Gender, n (%)	
Male	66 (31.1)
Female	146 (68.9)
Occupation, n (%)	
Traders	101 (47.6)
Others	35 (16.6)
State officials	23 (10.8)
Unemployed	18 (8.5)
Retirees	18 (8.5)
Employees in the private sector	17 (8.0)
Marital status, n (%)	
Married	103 (48.6)
Widowed living alone	42 (19.8)
Single	36 (17.9)
Divorced	29 (13.7)
Widowed remarried	2 (0.9)
Education level, n (%)	
None	65 (30.6)
Primary	60 (28.3)
Secondary	77 (36.4)
Higher study	10 (4.7)

Residential area, n (%)	
Urban	177 (83.5)
Rural	35 (16.5)
Smoker, n (%)	10 (4.7)
History of Diabetes, n (%)	8 (3.8)
History of HBP, n (%)	35 (16,5)
HAART exposure, n (%)	
Naifs-HAART	26 (13.3)
HAART-exposed	186 (87.7)
HAART regimen, n (%)	
2NRTIs+1NNRTIs	162 (87.1)
2NRTIs+1IPs	24 (12.9)
TDF Exposed, n (%)	169 (90.9)
AZT Exposed, n (%)	2 (1.1)
ABC Exposed, n (%)	15 (8.1)
EFV Exposed, n (%)	161 (86.6)
NEV Exposed, n (%)	1 (0.5)
ATV(r) Exposed, n(%)	24 (12.9)
Median duration of HAART exposure [Years (IQR)]	3.6 (2.7-7.1)
Median duration since HIV diagnostic [Years (IQR)]	4.1 (2.7-7.2)
CD4 count cel/mm^3,mean±SD	462 (±252)
CD4 count ≥ 500cel/ mm^3, n (%)	81/197 (41.1)
Viral load suppressed, n (%)	148/176 (84.1)

ABC: Abacavir; ATV(r) : Atazanavir boosted by Ritonavir ; AZT: Zidovudine; BMI : Body Mass Index ; EFV: Efavirenz; HAART: Highly active antiretroviral therapy; HBP: High Blood Pressure; IPs :Protease Inhibitors; NEV: Névirapine; NNRTIs: Non-nucleoside reverse transcriptase inhibitors; NRTIs: Nucleoside reverse transcriptase inhibitors ; SD: Standard deviation; IQR: Interquartile range

4.2 Cardiovascular risk factors Data

The median waist circumference was 85.5 cm (IQR: 79-93.2). The average body mass index was 23.9 Kg / m² (± 4.5). Among the cardiovascular risk factors, abdominal obesity was the most represented in 56.1% followed by HCH in 52.4% and hypertension in 44.8% (Table 2). Seventy-two point five percent of the patients had at least one dyslipidemia. Patients whose body mass index was ≥ 25 Kg / m² accounted for 36.3%. Women had significantly more abdominal obesity ($p<0.001$), more overweight ($p<0.001$), more HCH ($p<0.001$) and were more likely to have dyslipidemia ($p = 0.016$) than men. There was no significant gender difference in the frequencies of hypertension, HTG, HCT, HCL (Table 2).

Table 2: Characteristics of cardiovascular risk factors

	Overall (n=212)	Male (n=66)	Female (n=146)	p-value
Waist circumference [cm (IQR)]	85.5 (79-93.2)	82.3 (79-90)	87.5 (80-94)	0.019
Abdominal obesity, n (%)	119 (56.1)	12 (10.1)	107 (89.9)	<0.001
SBP[mmHg (IQR)]	130 (120-144)	131.5 (123-139)	129 (118-146)	NS

DBP[mmHg (IQR)]	84 (76-93)	84(78-93)	83 (76-94)	NS
HTA, n (%)	95 (44.8)	25 (37.9)	70 (47.9)	NS
BMI (Kg/m²), mean±SD	23.9 (±4.5)	22.3 (±3.3)	24.6 (±4.8)	<0.001
BMI Classification (Kg/m²), n(%)				
<18,5	21(9.9)	7(3.3)	14 (6.6)	0.012
18.5-24.9	114 (53.8)	45(21.2)	69 (32.5)	
25-29.9	61 (28.8)	14(6.6)	47 (22.2)	
30-34,9	9 (4.2)	0(0.0)	9 (4.2)	
35-39,9	7 (3.3)	0(0.0)	7 (3.3)	
CT [g/l(IQR)]	1.8 (1.6-2.1)	1.78 (1.4-2.1)	1.84 (1.6-2.1)	NS
HDL-c [g/l(IQR)]	0.5 (0.4-0.5)	0.5 (0.4-0.5)	0.5 (0.4-0.5)	NS
LDL-c [g/l(IQR)]	1.16 (0.9-1.4)	1.14 (0.8-1.4)	1.17 (1.0-1.6)	NS
TG [g/l(IQR)]	0.9 (0.6-1.2)	0.9 (0.7-1.3)	0.9 (0.6-1.1)	NS
Glycemia [g/l(IQR)]	0.9 (0.8-1.0)	0.9 (0.8-1.0)	0.9 (0.8-1.2)	NS
HDL-c < 0.4 g/l in men and < 0.5 g/l in women				
Yes	111(52.4)	21 (18.9)	90 (81.1)	<0.001
TG ≥ 1.5 g/l, n (%)				
Yes	24 (11.3)	10 (41.7)	14 (58.3)	NS
LDL-c ≥ 1.3 g/l, n (%)				
Yes	66 (31.1)	21 (31.8)	45 (68.2)	NS
CT ≥ 2.0 g/l, n (%)				
Yes	64 (30.2)	20 (31.2)	44 (68.8)	NS
Any dyslipidemia, n (%)	148/204 (72.5)	40 (27.0)	108 (72.9)	0.016

BMI: Body Mass Index ; CT: Total Cholesterol; DBP: Diastolic Blood Pressure; HDLc: HDL- Cholesterolemia; IQR: Interquartile range; LDLc: LDL Cholesterolemia; NS: Not significant; SBP: Systolic Blood Pressure; SD: Standard deviation; TG: Triglyceridemia.

4.3 Cardiovascular risk Evaluation and level of agreement between the different scores

Median CVR was 6.3% (IQR: 3.9-11.2), 0.0% (IQR: 0.0-1.0), 4.0% (IQR: 3.0-8.0), 3.0% (IQR: 1.95-5.01), based on Framingham score, SCORE risk, WHO score and D.A.D score respectively. The overall cardiovascular risk evaluation ranked 8% of patients at high cardiovascular risk, 25% at moderate risk and 67% at low risk according to the Framingham score. The distribution according to SCORE was 6.1% of patients classified at high risk, 3.3% at moderate risk and 90.6% at low risk. The WHO risk score classified 5.2% high risk, 10.8% moderate risk and 84% low risk. Finally, the D.A.D score classified 1.5% of patients as high cardiovascular risk, 4.2% as moderate risk and 94.3% as low risk. (Table 3).

Table 3: Distribution of the study population according to the different cardiovascular risk scores

		Framingham (N=212)	ESC/SCORE (N=212)	WHO non laboratory based charts for Western Sub-Saharan Africa (N=212)	D.A.D (N=212)
Risk level	Low, n (%)	142 (67.0)	192 (90.6)	178 (84.0)	200 (94.3)
	Moderate, n (%)	53 (25.0)	7 (3.3)	23 (10.8)	9 (4.2)
	High, n (%)	17 (8.0)	13 (6.1)	11 (5.2)	3 (1.5)

D.A.D : Data Collection on Adverse Effects of Anti-HIV Drugs; WHO: World Health Organisation; ESC/SCORE: Systematic Coronary Risk Evaluation of European Society of Cardiology.

There was a strong positive and statistically significant correlation between the CVR scores based on the general population and the scores obtained according to the D.A.D algorithm as illustrated in Figure 1: Framingham and D.A.D ($r=0.80$; $p<0.001$) ; SCORE and D.A.D ($r=0.58$; $p<0.001$) ; OMS and D.A.D ($r=0.65$; $p<0.001$).

The level of agreement between the Framingham score and the D.A.D score was 71.2% ($\kappa = 0.19$ CI: 0.09-0.29; $p<0.001$). The SCORE risk and the WHO score presented respectively with the D.A.D score a level of agreement of 89.6% ($\kappa = 0.28$ CI: 0.12-0.43; $p<0.001$) and 83.9% ($\kappa = 0.21$ CI: 0.06-0.35; $p<0.001$) as shown in Table 4.

V. DISCUSSION

Very few studies on the evaluation of CVR in PLWHIV exist in Africa, especially those that compare CVR estimation scores specific to the population of PLWHIV with CVR estimation scores used in practice for the general population. The originality of our study lies in two aspects: firstly, to our knowledge, our study is the first of its kind to evaluate CVR among PLWHIV in Togo but also it is the first in Togo to compare, within an African population of PLWHIV, three CVR estimation scores developed for a general population with a score specific to PLWHIV.

The median age in our sample was 50.2 years (IQR: 44.8-56.0). Our result is close to that of Muiru et al. in Uganda [27] and Begovac et al. in Serbia [28] who reported median ages of 49 years in their respective series. However, our median age was higher than that reported in Turkey by Korten et al. i.e. 48 years [29].

Cardiovascular risk factors, the most represented in our study were abdominal obesity with a frequency of 56.1%, followed by HCH in 52.4% of cases and hypertension in 44.8%. The frequency of abdominal obesity that we objectified is higher than that reported by Edward et al. in Nigeria [30], Mashinya et al. in South Africa [31] who reported 13.1% and 23.9% respectively. In contrast, Policarpo et al. reported a significantly higher frequency of abdominal obesity of 46.7% in subjects over 40 years of age compared to patients under 40 years of age, 25.4% of whom were abdominally obese [32]. Contrary to our study where HCH was the second most represented CVD risk factor, it occupied the first place in the series of Mashiya et al. and Edward et al. with lower rates of 43.8% and 49.8% respectively and a higher rate in the series by Nery et al. i.e. 61.9%[30,31,33]. The variabilities in the literature relating to abdominal obesity and dyslipidemias could be attributed to genetic variability and different diets specific to the different ethnic groups included in the studies. This is the case of hypertriglyceridemia found at low rates in our

study (11.6%) also reported in other African studies [30,31,34] and which contrasts with high rates ranging from 36.4% to 61.4% in non-African studies [32,33]. There is a triglyceride paradox that may explain why blacks and people of African descent tend to have a low prevalence of HTG despite the presence of a high frequency of HCH [35]. One of the explanations would be hyperactivity of the lipoprotein lipase whose activity is not inhibited by insulin resistance and the low level of apolipoprotein CIII whose activity inhibits lipoprotein lipase activity in black compared to Caucasian [36].

The frequency of arterial hypertension that we have objectified was above the prevalence of hypertension reported in Togo in the general population which varies between 25 and 36.7% [37–39] and slightly exceeded the prevalence of hypertension in sub-Saharan Africa [40]. Begovac et al. in Serbia, Policarpo et al. in Portugal, and Korten et al. in Turkey reported in their series on PLWHIV subjects aged 40 and above, hypertension frequencies lower than our result, namely 31.5%, 24%, 22% respectively [28,29,32].

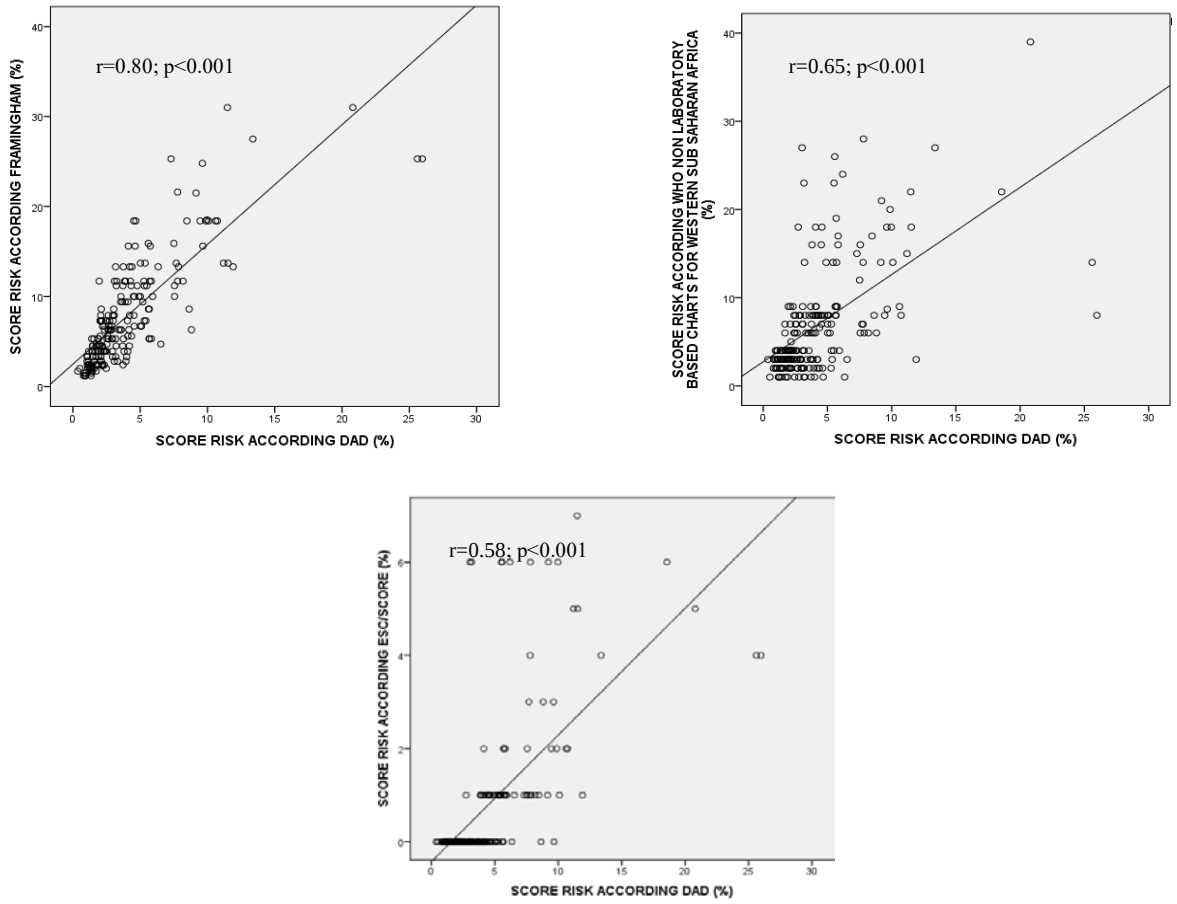

Figure 1: Correlation study between cardiovascular risks according to DAD with the FRAMINGHAM score the WHO score and the SCORE score

Table 4: Assessment of the level of agreement between the Framingham score, SCORE, OMS and the D.A.D score

Cardiovascular disease risk		Framingham (N=212)			ESC/SCORE (N=212)			WHO non laboratory based charts for Western SubSaharan Africa (N=212)		
		Low risk	Moderate	High	Low risk	Moderate	High	Low risk	Moderate	High
D.A.D (N=212)	Low risk	142	47	11	188	4	8	174	19	7
	Moderate	0	6	3	4	1	4	3	3	3
	High	0	0	3	0	2	1	1	1	1
Agreement			71.2%			89.6%			83.9%	
Kappa (p-value)			0.19 (<0.001)			0.28 (<0.001)			0.21 (<0.001)	
95%IC			0.09-0.29			0.12-0.43			0.06-0.35	

D.A.D : Data Collection on Adverse Effects of Anti-HIV Drugs; WHO: World Health Organisation

This high frequency of hypertension in our series could be explained by the stress to which the majority of patients in our study are exposed, firstly with regard to their sectors of activity which are based on small informal businesses that are unstable in terms of income but also because of the fear of the stigmatization linked to the status of PLWHIV which puts them in a situation of psychological tension each time they have to go to the hospital to renew their HAART. Indeed, stress and socio-professional categories have been reported to be associated with hypertension [41,42]. In addition, etiopathogenic predispositions related to lower renin activity, a high water-sodium retention coefficient and a probable higher prevalence of hyperaldosteronism have been reported as possible explanations for the susceptibility of the sub-saharan African subject to develop hypertension [43–48].

According to our results, CVR was high in 8% of the study population according to the FRS score, in 6.1% according to SCORE while the D.A.D score categorized 1.5% of the study population with high CVR. These rates reveal a low prevalence of subjects with high CVR in our sample. The estimated CVRs in the literature vary greatly depending on the estimation scores that were used. Indeed, the majority of studies in the literature have compared the 5-year estimated CVR according to D.A.D with the 10-year absolute CVR of the general population equations (Framingham, PROCAM, SCORE). Because the change over time in absolute CVR is not entirely linear, CVR based on estimation scales with different time projection variables may generate a lower probability of a perfect match leading to possible estimation biases [34].

However, it can be noted that some authors have reported, as we have, low rates of patients with high CVR in their series. This is the case of Noumegni et al. in Cameroon who reported in their series a proportion of RCV according to FRS close to our result (8.4%) and a slightly high proportion of 2.4% according to D.A.D [34]. Also in Brazil, Nery et al. reported low frequencies of subjects with high CVR: 2.8% according to FRS and 2.1% according to D.A.D [33]. In contrast, Begovac et al. in Serbia reported high frequencies of subjects with high CVR namely 27.16% according to FRS, 31.49% according to SCORE, and 51.6% according to D.A.D [28]. Similarly, Dhillon et al. in the United Kingdom reported high frequencies of subjects with high CVR of 21.5% according to FRS and 14.8% according to D.A.D as well as Policarpo et al. in Portugal with 20.5% according to FRS, 10.3% according to D.A.D, 4.4% according to SCORE [32,49]. The high rates of subjects with high CVR objectified by certain scores in these European studies could be explained by the high frequency of smoking 24.4%, 42.9%, 51.9% respectively in the studies by

Dhillon et al., Begovac et al. and Policarpo et al. against 4.7% in our study.

Our study allowed us to demonstrate a strong positive correlation between the three CVR estimation scores reserved for the general population FRS, SCORE, WHO in the CVR estimation with the D.A.D. Noumegni et al. reported, as we did, a positive correlation between the FRS equation and D.A.D score.

However, despite the excellent continuous positive correlation displayed between the general scores and the D.A.D score, the level of agreement between the Framingham score and the D.A.D score was slight (κ = 0.19 CI: 0.09-0.29; p<0.001) while SCORE (κ = 0.28 CI: 0.12-0.43; p<0.001) and the WHO CVR score (κ = 0.21 CI: 0.06-0.35; p<0.001) showed a fair level of agreement. In contrast to our result, a fair level of agreement between the FRS score and the D.A.D score was reported by Nery et al. (κ = 0.23), Pirs et al. (κ = 0.24), Mashinya et al. (κ = 0.23), while a substantial level of agreement between these two scores was reported by Noumegni et al. (κ = 0.61) [30.32.33.49]. For Pirs et al. the level of agreement was rather moderate (κ = 0.53) between SCORE and D.A.D [50].

The SCORE risk and the WHO rating scale showed approval rates of 89.6% and 83.6% respectively with the D.A.D score well above the 71.2% approval rate of the FRS score. In addition, the WHO CVR estimation table categorized 5.2% of the study population as having high RCV, a rate which is close to the rate estimated by SCORE (6.1%). Based on these results, it can be suggested that the evaluation of the CVR according to the WHO, not taking into account laboratory data, may constitute an acceptable tool at a lower cost to estimate CVR in PLWHIV without cholesterol level measurement in low income countries such as Togo. However, if serum cholesterol measurement is available, evaluation using SCORE could be a suitable alternative. But, it should be kept in mind that out of the cumulative frequencies of patients classified as moderate and high CVR, 40% (8/20) and only 23.5% (8/34) respectively according to SCORE and WHO were finally classified as moderate and high CVR according to the D.A.D algorithm. This result shows that these two scores overestimate the CVR as well as the FRS, of which only 17.1% (12/70) of the cases classified as moderate and high risk were classified by D.A.D (Table 4). Noumegni et al. and Edwards-Jackson et al. also reported that the trend in FRS score, overestimated CVR in PLWHIV. In practice, this means that some patients may be classified as high CVR and excessively benefiting from intensive CVD prevention measures. This would expose patients to potential adverse drug reactions, but also to increased health costs. A solution that could sort this out for this purpose would be the measurement of media thickness / intima of the carotid artery, which would make it possible to identify among the subjects considered to be at moderate risk according to SCORE and the WHO estimation scale, those with a real high CVR. SCORE risk and the D.A.D scale have demonstrated a good ability to identify patients with subclinical atherosclerosis [50] although it should be noted that according to another study, D.A.D and SCORE underestimated the presence of subclinical atherosclerosis and that D.A.D outperformed SCORE in detecting subclinical atherosclerosis [51].

Our study has limitations that are worth noting. Firstly, the cross-sectional nature of our study does not allow us to establish a cause and effect relationship between the vascular risks estimated by the various scores that were the subject of our study and the actual cardiovascular events expected or which will occur. Only an observational study could answer this question. Secondly, our study was based on patients with unknown cardiovascular pathologies followed in an urban center. Thus, our sample may not be representative of the entire Togolese population living with HIV. Nevertheless, our study has the merit of being the first to attempt to evaluate CVR using four CVR scores. Therefore, its results constitute data that can be compared with those of middle and high income countries. Thirdly, our analysis only included patients aged 40 years and older, so the estimated frequencies of CVR could be different if younger subjects were included.

However, the age range we used is the age range in which the different CVD risk equations were primarily developed and validated. Fourth, excluding patients on lipid-lowering drugs probably contributed to the exclusion of subjects with other potential CVD risk factors which may have lowered CVR levels. Finally, we did not evaluate fat distribution disorders, lipodystrophy and lipoatrophy that have been shown to be associated with elevated CVR.

VI. CONCLUSION

The overall CVR estimated by the different CVR estimation scores allowed us to highlight a low frequency of PLWHIV with high CVR in our sample. However, high frequencies of well-known CVD risk factors such as hypertension, HCH, abdominal obesity to which are added the increase in the average age of PLWHIV require caregivers in charge of medical monitoring of PLWHIV not to content to only monitor the CD4 count and viral load but also to systematically take into account the evaluation of the global CVR in patients. To this end, as far as Togo is concerned, the WHO scale taking into account only the clinical parameters devoted to sub-Saharan Africa can be a very practical and low cost alternative tool. If, however, a measure of total serum cholesterol is available, the SCORE scale may be more appropriate. Detecting subjects with high CVR is essential in order to institute preventive measures to reduce risk, starting with the management of CVD factors and adopting a healthy lifestyle.

Conflicts Of Interest:

The authors declare that they have no conflict of interest.

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Lake Placid in Hypopharynx: Retropharyngeal Abscess from Retrieved Fish Bone

Gerald Parisutham Sebastian MS,Rajeswari Subbarayan MS Selvarajan Nagarajan MS & Anju Radhakrishnan MS

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ABSTRACT

Fish bones are common foreign bodies encountered in the throat. Fish bones may migrate in any direction if they are not removed early. Rarely, they are embedded in the soft tissue causing abscess (RPA) formation. RPA needs prompt diagnosis and early management which often requires surgical drainage to achieve optimum result. The diagnosis is based on clinical and radiological pictures. The management needs securing of the airway, surgical drainage and antibiotics. We report a case of RPA after removal of ingested foreign body of fish bone.

Keywords: acute retropharyngeal abscess, fish bone, airway.

Classification: NLMC Code: QW 70

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ABSTRACT

Fish bones are common foreign bodies encountered in the throat. Fish bones may migrate in any direction if they are not removed early. Rarely, they are embedded in the soft tissue causing abscess (RPA) formation. RPA needs prompt diagnosis and early management which often requires surgical drainage to achieve optimum result. The diagnosis is based on clinical and radiological pictures. The management needs securing of the airway, surgical drainage and antibiotics. We report a case of RPA after removal of ingested foreign body of fish bone.

Keywords: acute retropharyngeal abscess, fish bone, airway.

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I. INTRODUCTION

Deep neck spaces are the potential spaces bounded by the layers formed by cervical fascia. They are named according to their anatomical location such as parapharyngeal space, retropharyngeal space, peritonsillar space, etc. Infections involving any one of these spaces may spread into anothThe complications relating to the ingestion of foreign bodies, such as retropharyngeal abscess, are of low prevalence, but potentially severe. The commonest features are odynophagia, neck swelling and fever, but respiratory distress is considered to be rare[2]. If the abscess not detected early, patients may progress rapidly into respiratory distress because the symptoms are directly proportionate with the volume of abscess[3]. The clinical symptoms and lateral neck X-rays were sufficient to diagnose RPA[4]. Once diagnosed, it is prompted for immediate securing the airway and emergency drainage as impending compromise of the airway may prove to be fatal. We reported here a case of RPA after removal of ingested foreign body of fish bone.

II. CASE REPORT

A 11 year old female child referred from paediatrician with complaints of progressive painful neck swelling,odynophagia and fever for 5 days. It was associated with difficulty in swallowing and restriction of neck movements. There was a history of Rigid esophagoscopy and foreign body removal of fish bone (Fig. 1) under general anaesthesia 6 days ago in private hospital following which patient was discharged on post operative day 1 with oral Antibiotics and Analgesics coverage.

On general examination, child appeared febrile and fairly lethargic she was in mild respiratory distress and in impending stridor. Her blood pressure and oxygen saturation were within the normal range. Throat examination is not done in view of impending stridor. The right side of the neck was firmly swollen and tender with loss of Laryngeal crepitus and mobility of neck was restricted for extension.. Laboratory analysis revealed an elevated total white cells count of 23 X 10^3 with predominant neutrophils. Plain lateral soft tissue radiograph of the neck showed markedly widened prevertebral soft tissue shadow with air fluid level along the cervical region with the loss of normal cervical lordosis (Fig. 2). Then we requested an emergency computed tomography (CT) of neck that confirmed large retropharyngeal abscess extending from C3 up to D1 measuring 6*4*10 cm

with mild airway compromise . CT chest is also done which ruled out COVID 19 infection, aspiration pneumonitis and mediastinitis.The intravenous antibiotic (Piperacillin Tazobactam with metronidazole), and intravenous dexamethasone started and she was put on nasal prong oxygen therapy. The patient was closely observed in the ward and after obtaining proper informed written consent including High risk and death on table consent for the emergency procedure, patient was prepared for the emergency Rigid Oesophagoscopy examination & incision and drainage under General anaesthesia in the Emergency operation theatre.

Then the child was shifted to emergency operation theatre,General Anesthesia given through Orotracheal intubation done with 6 size cuffed ET tube by experienced anaesthetist. A paediatric upper end Rigid oesophageal speculum introduced per orally and navigated through oropharynx. A smooth bulge noted in the posterior pharyngeal wall extending upto right pyriform sinus. A small vertical incision made in inferior aspect of the bulge and 20-30 ml of thick greenish pus gushed out.

The same was suctioned out and sent for pus culture and sensitivity. A paediatric rigid esophagoscopy was navigated through cricopharynx upto thoracic oesophagus.

No significant abnormality or foreign body visualized. Then the child was repositioned in Sister Rose position. Boyle Davis mouth gag with appropriate size Doughty's Tongue blade introduced and mouth opened and fixed with Draffin's bipod. A smooth bulge visualized in the posterior pharyngeal wall. A vertical incision made at the point of maximum bulge by sickle knife. A dry air released with 5-10 ml of pus was suctioned out. Perfect haemostasis obtained. Boyle Davis mouth gag removed. Ryles tube insertion done and position confirmed. Child recovered from general anaesthesia and extubated smoothly and shifted to post operative recovery room for vitals monitoring.

Then emergency Paediatrician review obtained postoperatively for proper Antibiotic spectrum.. Then the patient was continued with intravenous antibiotics and analgesics.. The culture report revealed a growth of Enterococcus species.

On post operative day 1, Ryles tube feeding started after taking check x ray lateral view Neck and x ray chest. The patient reviewed clinically t on 5th post operative day with check x ray lateral view showed collections in the retropharyngeal area. So again child is taken up for revision incision and drainage on 6th post operative day, about 1ml of pus drained. With control CT in the 10th postoperative day with no collections or edema, patient was discharged on the 10th postoperative day after starting oral diet.

III. DISCUSSION

In children, RPA is a less common type of deep neck infection after parapharyngeal and submandibular abscesses. Gender wise, the boys were predominantly involved (63%), while the peak incidence occurred before the age of 3 (42%) followed by the age group of 4-11(28%). This age distribution can be contributed to the fact that in children below 5 years of age, the presence of paramedian group of lymph nodes which provide a common drainage pathway from nasopharynx, nose, paranasal sinuses, adenoids and tonsils may become the source of infection and the formation of abscess was mainly due to the suppuration of these lymph nodes. They commonly involuted by the age of 5.

It is supported by the studies which showed that the commonest antecedent factor were upper respiratory tract infection (eg; rhinosinusitis (30%), tonsillitis (17%) while ingestion of foreign body or pharyngeal trauma (25%) also have been reported[5].

Infections that affect the retropharyngeal space may be generated by the contiguity or be secondary to penetrating trauma.In the first case, there may occur suppuration of retropharyngeal lymph nodes that drain upper airways infections or extension from the affection of other cervical spaces. In the second way, the infection is secondary to a penetrating trauma, that may be a foreign body ingestion and even an iatrogenic

injury by Flexible or Rigid endoscopy, orotracheal intubation, laryngoscopy and passage of the nasogastric tube[6].

The symptoms upon presentation were variable. Grisaru Soen et al., reported among 39 patients they studied, the commonest triad of symptoms were fever, neck pain and dysphagia while only 2 patients (5%) manifested stridor. Other study by Nazir et al., reported only 6 of the 40 patients had stridor while Laughlin et al., reported 29% of the patients studied presented with respiratory compromise. These studies showed that signs of airway compromise are uncommon for RPA at presentation in some cases. The security of the airway is important and endotracheal intubation is indicated if the airway obstruction is severe. In this case, we did not electively secure the airway at the time of presentation as it was not indicated.

As the potentially fatal outcome is waiting, the fast and accurate diagnosis is precious. The lateral soft tissue neck X ray is a simple yet useful screening tool in the diagnosis of RPA with the 80% sensitivity[7].

Criteria to suggest an RPA include thickening of the prevertebral soft tissue of more than 50% from the width of any cervical vertebral body, the loss of normal cervical lordosis and the presence of gas or fluid level in the prevertebral shadow. All of the features described were evidently seen in this patient lateral neck x-ray (Fig. 2). The surgical drainage is the recommended treatment in RPA when there is evidence of compromised airway while empirical antibiotic of broad spectrum should be started promptly.

IV. CONCLUSION

Fish bone is often encountered as a foreign body in upper digestive tract. This clinical situation is favourable when the diagnosis and its removal are made in time. The occurrence of complications, even after removal of foreign body, particularly retropharyngeal abscess is an extremely rare one with a high mortality and morbidity. It is essential to monitor the post operative patients of foreign body removal with appropriate antibiotics followed by clinical, laboratorial and radiological investigations. Early diagnosis and prompt treatment of retropharyngeal abscess are essential for preventing catastrophic complications. In this case study it has been proved that minimum antibiotic coverage for 1 week is essential to avoid post foreign body removal complications like retropharyngeal abscess. Despite numerous challenges encountered during the management of our patient, the end result was satisfactory and life saving.

Author's Contributions:

Selvarajan Nagarajan: contribution to content, design of manuscript, literature search, data analysis and interpretation.

Rajeswari Subbarayan: contribution to content, design of manuscript, literature search, data analysis and interpretation.

Anju Radhakrishnan: contribution to preoperative preparation and postoperative follow up

Gerald parisutham Sebastian: contribution to content, design of manuscript, literature search, data analysis and interpretation. Revision and correction of manuscript for submission. *Disclosure:*

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None

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District ethical committee-Institutional ethical committee permission exempted.

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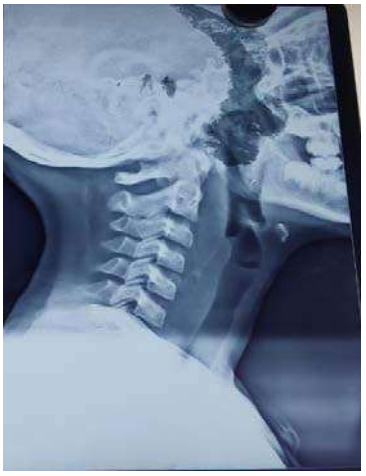

Figure 1: Radioopaqueforeign body in the cricopharynx at the level of C3 and C4 level

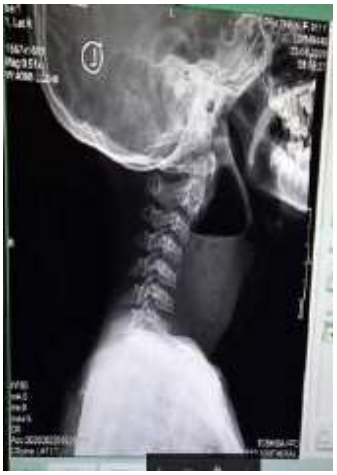

Figure 2: Plain lateral soft tissue radiograph of the neck showing markedly widened prevertebral soft tissue shadow with air fluid level along the cervical region with the loss of normal cervical lordosis

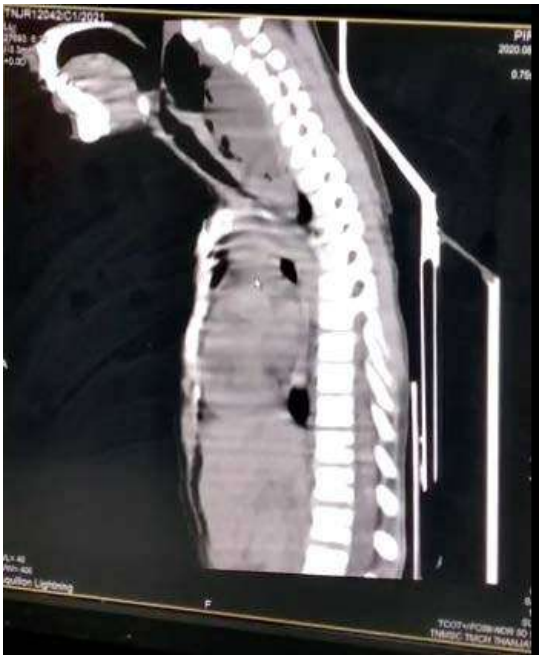

Figure 3: A large retropharyngeal abscess extending from C3 upto D1 measuring 6*4*10 cm with mild airway compromise

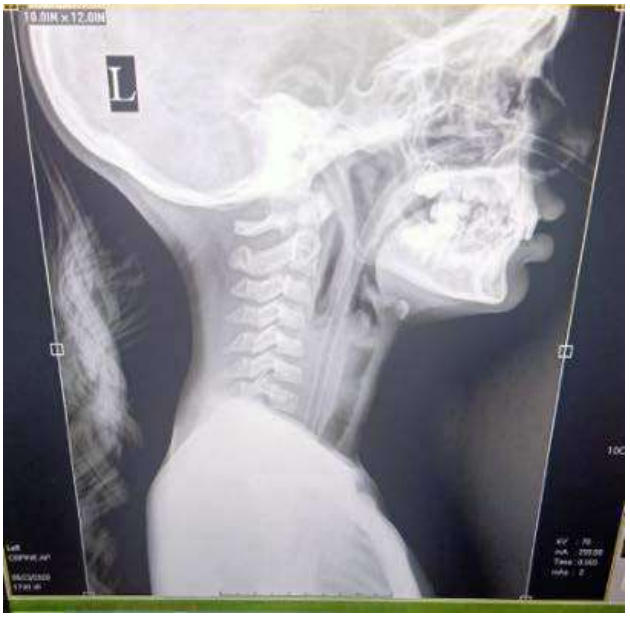

Figure 4

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Multiple Sclerosis- A Boon or a Bane in Pregnancy??

Dr. Sharanya

ABSTRACT

Introduction: MS is the most common acquired neurologic disorder of young adults, with at least 2.5 million individuals affected worldwide. There is a female preponderance of 3:1. This gender bias will become more pronounced, because MS is on the rise among young (reproductive age) women. It typically occurs between 20 to 40 years of age.

Case Presentation: A 21 year old primigravida at 36+3 weeks of gestational age complaints of continuous pain in abdomen and dry cough without breathlessness since one day. She was a known case of multiple sclerosis. . At 26 weeks she consulted neurologist in St. Philomena's hospital in view of progressive lower limb weakness since 2 weeks and walk with support and was advised to start injection methylprednisolone pulse therapy and she improved in few weeks. At 36+3 weeks on examination her BP was 130/90 mmHg in right arm in supine position, other vitals were normal. Bilateral basal crepts were present on chest auscultation and mild IUGR noted per abdomen. Her BP continued to be between 130/90 to 140/90 mmHg , urine albumin 2+ , PIH profile were normal, multidisciplinary approach was taken and she was started on tablet labetalol. Patient had imminent signs and symptoms hence decision for emergency LSCS taken. Patient threw GTCS with frothing from mouth While taking up for emergency caesarean section, injection MgSo4 loading dose given and continued as per Pritchard regimen, emergency caesarean done.

Discussion: Multiple sclerosis is an idiopathic, chronic inflammatory disease of the central nervous system characterised by multiple plaques of demyelination in the brain and spinal cord. There are many possible causes of MS, including viruses, autoimmune disorders, environmental factors and genetic factors.In MS, the immune system commonly attacks its own nervous tissue. Symptoms include muscle weakness in the extremities, difficulty with coordination, spasticity, fatigue, loss of sensation, seizure, speech impediments, bowel and bladder dysfunction.

Keywords: multiple sclerosis, neurological, breath- lessness, weakness.

Classification: NLMC Code : WL 360

Language: English

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Keywords: multiple sclerosis, neurological, breath- lessness, weakness.

Author: Post Graduate, MBBS, DNB- III year St Philomena's Hospital, Bengaluru.

I. INTRODUCTION

MS is the most common acquired neurologic disorder of young adults, with at least 2.5 million individuals affected worldwide. There is a female preponderance of 3:1. This gender bias will become more pronounced, because MS is on the rise among young (reproductive age) women. It typically occurs between 20 to 40 years of age. Specific management questions and concerns surround the pre pregnancy, pregnancy and postpartum period. Unfortunately, there are no recognized and implemented guidelines.[1]

II. CASE PRESENTATION

A 21-year-old primigravida at 36+3 weeks of gestational age was admitted to St.

Philomena's hospital in December 2019 with complaints of continuous pain in abdomen and dry cough without breathlessness since one day. She was admitted in 2014 with complaints of diplopia and right upper limb weakness, investigated and diagnosed with multiple sclerosis in NIMHANS Bengaluru. She was initially treated

with injection methylprednisolone pulse therapy and was put on tablet prednisolone in tapering

doses over 6 months and tablet Azathioprine which was stopped prior to conception. At 26 weeks she consulted neurologist in St. Philomena's hospital in view of progressive lower limb weakness since 2 weeks and walk with support and was advised to start injection methylprednisolone pulse therapy and referred to us for obstetrical care, she continued regular antenatal visit, her blood sugar and BP were normal throughout, her lower limb weakness improved gradually and she was started walking without support over a period of 3 weeks. On admission at 36+3 weeks on examination her BP was 130/90 mmHg in right arm in supine position, other vitals were normal. Bilateral basal crepts were present on chest auscultation and mild IUGR noted per abdomen. Her BP continued to be between 130/90 to 140/90 mmHg , urine albumin 2+ , PIH profile were normal, multidisciplinary approach was taken and she was started on tablet labetalol. Steroid prophylaxis for foetal lung maturity given. After 5 hours of admission patient started complaining of breathlessness, respiratory rate was 22/minute, SpO2 was 98% on room air and bilateral basal crepts were present, chest x ray was suggestive of Para cardiac pneumonitis and was started on injection Co-trimoxazole, Azithromycin, Levosalbutamol & Ipratropium bromide and Budesonide nebulization. 2-D echocardiography was suggestive of mild MR, mild AR, grade II TR with moderate PAH, LVDD-1, EF- 60% with mild pericardial effusion. Tablet Labetalol was hiked and tablet Nicardia-retard added in view of rising and uncontrolled BP.

Patient had imminent signs and symptoms hence decision for emergency LSCS taken. Patient threw GTCS with frothing from mouth While taking up for emergency caesarean section, injection MgSo4 loading dose given and continued as per Pritchard regimen, emergency caesarean done, baby cried at birth with 1.87kg.

Patient was shifted to ICU for close monitoring. In view of rising total leucocyte count and falling platelets, antibiotics were upgraded. CT abdomen and pelvis done to look for focus of infection which was normal. Post operatively Inj. Levetiracetam started by neurologist, on post-op day 2, 1 pint packed cell transfused in view of low haemoglobin, patient's condition was improving. Patient was stable and hence discharged on post operative day 7. Patient followed up in OPD after discharge and was symptomatically improved.

III. DISCUSSION

Multiple sclerosis is an idiopathic, chronic inflammatory disease of the central nervous system characterised by multiple plaques of demyelination in the brain and spinal cord. There are many possible causes of MS, including viruses, auto immune disorders, environmental factors and genetic factors. In MS, the immune system commonly attacks its own nervous tissue. Symptoms include muscle weakness in the extremities, difficulty with coordination, spasticity, fatigue, loss of sensation, seizure, speech impediments, bowel and bladder dysfunction. Studies have shown that uncomplicated MS has no apparent effect on fertility, pregnancy, delivery and congenital abnormalities and stillbirth [2].One study of a large U.S. national database noted marginally increased risk of foetal intrauterine growth restriction and rate of caesarean section[3]. In a small study, researchers cautiously predict an increased relapse rate in patients with MS undergoing in vitro fertilization. This effect was noted for 3 months after the procedure, possibly associated with failure of IVF and the use of Gonadotropin Releasing Hormone agonists [4]. The disabling effects of the disease may make it difficult for the mother to carry a pregnancy, therefore more frequent prenatal visits may be needed for close monitoring of the disease and of foetal wellbeing. There is no established treatment that alters the course of MS. There is no established treatment that alters the course of MS. However medications may be used in pregnancy including steroids and anti-inflammatory drugs. There is no evidence showing increase risk of preeclampsia or eclampsia in pregnancy. Delivery of the baby may be difficult. While labour itself is not affected, the muscles and nerves needed for pushing can be affected. This may make caesarean section, forceps and vacuum assisted deliveries more likely.

Pregnancy does not appear to speed up the course or worsen the effects of MS and may be beneficial. Pregnancy is known to be associated with an increase in a number of circulating proteins, corticosteroids and other factors that are natural immunosuppressant. Some studies have found that MS symptoms decrease in pregnancy and increase during the postpartum period [5]. Exacerbation rates tend to rise in the first 3 to 6 months postpartum and the risk of a relapse in the postpartum period is estimated to be 20-40% [6]. For patients whose disease worsens and want to continue to breastfeed, glatiramer acetate and interferon beta are most likely to be safe.

Current recommendation is to stop disease-modifying therapy (DMT) such as glatiramer acetate, interferon beta-1a, and interferon beta-1b, teriflunomide, fingolimod, and dimethyl fumarate prior to a planned pregnancy and during breastfeeding due to lack of sufficient evidence for safety. The oral agents teriflunomide, fingolimod, and dimethyl fumarate cause reproductive toxicity in animals and are contraindicated during pregnancy and to employ strict contraception. Woman taking teriflunomide and planning pregnancy a "washout period" for as long as 2 years may be required before blood levels considered safe are obtained. Elimination of fingolimod takes about 2 months. The use of prednisolone and methylprednisolone for acute MS relapse in pregnancy is thought to be relatively safe (FDA category C).

IV. SUMMARY

Pregnancy does not appear to be associated with an adverse outcome in multiple sclerosis. There is a consensus supporting the observation that the nine months of pregnancy are associated with a reduction in the frequency of relapse, which is followed by an increase in the relapse rate in the initial 3 to 6 months postpartum.

Currently available evidence for the use of immunosuppressive agents in pregnancy is limited. The use of analgesia during delivery for patients with multiple sclerosis has not been extensively evaluated but there is no substantial evidence to suggest an increased risk of relapse.

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