IMAGE: A MAP OF THE STARS OF THE ORION CONSTELLATION

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ABSTRACT

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Keywords: plasma exchange, anxiety, sprague-dawley rat, elevated plus maze.

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Aging Blood Plasma Factors Support Anxiety-Like Behavior

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The naturally occurring aging process also causes metabolic and cognitive disorders. Studies report that young plasma factors have a rejuvenating effect on aged tissues and organs. However, there are limited studies investigating the effects of plasma factors on behavior. In this study, the effects of plasma exchange between young and old rats on anxious behavior were evaluated. The male Sprague-Dawley rat was chosen as the model organism. Blood plasma collected from 5-week-old rats was transferred to each of the 24-month-old rats at 0.5 ml per day for 30 days. The blood plasma collected from 24-month old rats was transferred to 5-week old young rats for the same period as 0.25 ml. After the plasma application, the elevated plus maze test, which is used to measure anxious behavior, was applied to the experimental and control groups. Statistical analysis of the obtained data showed that aged plasma factors cause anxious behavior in young rats. These results provide important evidence showing the profound effect of plasma factors, which weaken with aging, on cognitive processes.

Keywords: plasma exchange, anxiety, sprague-dawley rat, elevated plus maze.

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I. INTRODUCTION

Dysfunctions that develop at the organ and cellular level with the aging process lead to decreased quality of life with aging and accompanying diseases 1. With aging, blood plasma factors also change greatly and weaken (Kang and Yang, 2020). There are important parabiotic protein factors in the blood of young animals that can aid in rejuvenation. IGF-1 and Follistatin are defined as several of these "youth proteins" such as LIF, Leptin, Cerberus, GDF5, TIMP1, TIMP4, and their concentrations have been found to be negatively correlated with aging.

Various anti-aging factors, such as growth hormone-releasing hormone (GHRH), oxytocin, GDF11, TIMP2 and osteocalcin, can be found in young blood plasma. It has been reported that young plasma application reduces aging biomarkers such as ferric reducing ability (FRAP), plasma membrane redox system (PMRS) activity, GSH, malondialdehyde (MDA) levels, and protein carbonylation (PCO) in rat blood (Tripathi et al., 2021). A study of the mouse plasma proteome showed that several proteins and/or isoforms change significantly with age. It is emphasized that these proteins and/or isoforms can be used as biomarkers of aging in mice. Some of the related proteins (Prx-2 and Hp) are antioxidant proteins such as SAA-1 and TTR, while others are reported to participate in aging-related amyloid production in the vascular system with transport and metabolic functions. In addition, increased TTR production and decreased plasma albumin levels have been reported to be associated with age - related deaths and diseases. However, post-translational modifications of these blood proteins may also contribute to the aging process (Ding and Kopchick, 2011).

Studies have reported that young blood plasma factors increase the activation of muscle stem cells (Conboy et al., 2005). In another study, it was shown that muscle fibrosis decreased with increased Wnt signal of young blood systemic molecules (Brack et al., 2007). In addition, significant differences in juvenile skeletal muscle regeneration levels were observed in an injury model in an older person exposed to juvenile

blood plasma compared to an older person (Egerman et al., 2016). Young plasma has also been shown to reduce hepatic tissue regeneration by modulating age-related liver dysfunction and autophagy pathways (Liu et al., 2018). Studies indicate that other plasma proteins may contribute to brain aging by passing into the central nervous system (CNS) due to the damaged blood-brain barrier (BBB) (Kheifets and Braithwaite, 2019). Similarly, the curative effects of young blood are thought to be able, through largely unknown mechanisms, to go beyond the BBB to ameliorate age-related brain dysfunction, demonstrating curative effects in the brain at increased adult neurogenesis, improved hippocampal synaptic plasticity, and cognitive levels (Villeda et al., 2014). However, the blood-plasma factors of the elderly individual have a negative effect on the tissue and behavior of the young individual (Villeda et al., 2011). In this study, the effects of aged blood plasma factors on anxiety-like behavior in young rats are evaluated after blood plasma exchange between young and old rats.

II. MATERIAL AND METHOD

2.1 Animal studies

The research employed the male Sprague Dawley rat as a model organism. Aged rats (24 months, n = 7) received pooled plasma (0.5 ml daily for 30 days, intravenously into the tail vein) collected from young (5 weeks, n = 51) rats, and young rats (5 weeks, n = 7) received pooled plasma (0.25 ml daily for 30 days, intravenously into the tail vein) collected from aged (24 months, n = 16) rats. The elevated plus maze test was done on both the experimental rats and the rats in the control group one day after the plasma application. All animals were housed under standard animal care conditions and had free access to food and water.

This study was approved by the Saki Yenilli Experimental Animal Production and Practice Laboratory's Ethics Committee (permission number: 2021/03) (Ceylani and Teker, 2022; Villeda et al., 2014)

2.2 Plasma collection

Animals were rendered unconscious by short-term treatment with ether before blood samples were taken. Pooled rat plasma was collected by intracardial bleed at the time of euthanasia. Plasma was prepared from blood collected with EDTA, followed by centrifugation at 1,000 g. The plasma was denaturated by heating it for 2–3 minutes at 95 °C, followed by a short spin at 1,000 g. All plasma aliquots were stored at -80 °C until use. Before it was given, EDTA was taken out of the plasma using 3.5-kDa D-tube dialyzers (EMD Millipore) in PBS (Villeda et al., 2014).

III. BEHAVIORAL TESTS

3.1 Elevated plus maze test

Polyester apparatus for the elevated plus maze test, which is used to assess the level of anxiety in mice and rats. It consists of a platform (10×10 cm) in the center, two open arms (50×10 cm) and two (50×10 cm) arms covered with plastic glass 30cm high and consists of in the apparatus designed as a plus, open arms and closed arms face each other. The cross-shaped labyrinth consisting of four arms is at a height of 80 cm from the ground.

For each experiment, only one rat is placed in the center of the cross maze and allowed to explore the maze for five minutes. At the end of the given time, the time spent by the mouse in the open and closed arms and the numbers of entries in these arms are recorded with a computer-aided video system (Ceylani et al., 2018).

3.2 Statistics

The statistical analyses were given as mean ± standard error of the mean (SEM). Unpaired T-test (one-sided p-value) was utilized to compare the anxiety-like behavior between YO pls (blood plasma obtained from young rats was transferred to old rats) and YOcnt (control groub), OYpls (blood plasma obtained from old rats was transferred to young rats) and OYcnt (control groub) groups. The comparison was done in GraphPad Prism 9 (GraphPad Software, USA) software. The degree of significance was denoted as * $p < 0.05$ and ** $p < 0.001$.

IV. RESULTS AND DISCUSSION

Deformations that occur in tissues, organs, and systems with aging also negatively affect the cognitive processes of the person (Castellano, 2019). Different approaches that can play a role in the elimination of metabolic and cognitive disorders that aging requires are being evaluated.

A substantial amount of recent research has shown that intermittent fasting practices can be a powerful approach that can be preferred in eliminating the harm caused by aging (Ceylani et al., 2022; Teker and Ceylani, 2022). Another powerful biological agent that plays a role in the elimination of damage to tissues and organs in the aging process is young blood plasma (Pandika, 2019). Studies on the positive effects of young blood plasma factors have also revealed that aged plasma factors have negative effects in the opposite direction (Villeda et al., 2011). In this study, the effects of plasma exchange between young and old rats on anxiety-like behavior were investigated. Old plasma factors were found to cause anxious behavior in young rats.

The elevated plus maze has been characterized as a straightforward tool for evaluating rodent anxiety reactions. The elevated plus maze takes use of rodents' natural aversion to open spaces and heights as well as their predisposition to seek out dark, confined areas (approach) (avoidance) (Walf and Frye, 2007). It is possible to evaluate the impact of reproductive senescence or aging as well as prenatal, perinatal, or postnatal exposure to a variety of stresses. The elevated plus maze can be used as a behavioral assay to study brain sites such as hippocampus and amygdala and mechanisms such as hypothalamic–pituitary–adrenal axis (Belzung and Griebel, 2001). The results obtained in this study show that plasma exchange between young and old rats can play a decisive role in behavior. Although the time spent in the closed arms of the old rats to which young plasma was transferred was less than in the control group, there was no significant difference ($p = 0.3436$) Figure 1A. There was no significant difference in the time spent in the open arm ($p = 0.5037$) and in the center ($p = 0.6389$) of the old rats to which the young plasma was transferred. Figure 1B-C. There was also no significant difference in terms of transition between arms ($p > 0.9999$) Fig. 1D. However, young rats to whom aged plasma was transferred spent more time in the closed arm, with a significant difference compared to the control group ($P = 0.0099$) Figure 2A. Similarly, aged plasma significantly decreased the time spent by young rats in the open arm ($p = 0.0326$) Figure 2B. But there was no significant difference in terms of time spent in the center ($P = 0.0991$) and transition between arms ($P = 0.0532$) Figure 2C-D.

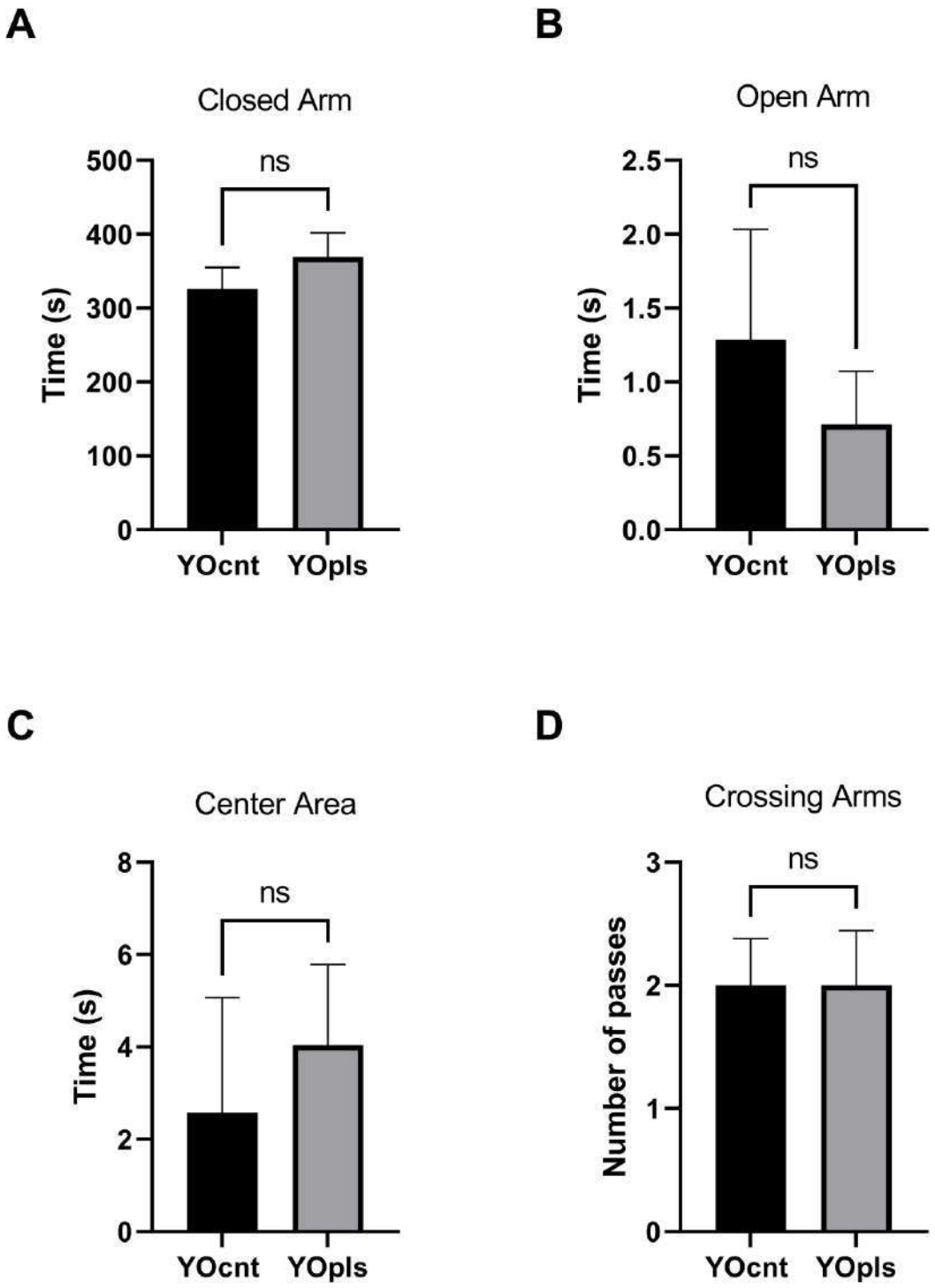

Figure 1: Statistical comparison of the time spent by old rats in the plus maze test apparatus after young plasma transfer: closed arm (A), open arm (B), center (C), and number of passes between closed arms (D)

It is seen that the focus of plasma exchange studies is mostly focused on revealing the positive effects of young plasma. While this situation draws attention to the importance of plasma factors, it also shows the negative effect of aging on plasma factors. Although it is promising that the rejuvenation caused by young plasma application at tissue and organ level has a positive

effect on behavior, it is not surprising. However, it is quite remarkable that the blood plasma of an old rat can have a negative effect on the behavior of a 5-week-old rat. Old mice receiving blood plasma from young mice have been shown to have increased synaptic activity and cognitive functions of the hippocampus (Khrimian et al., 2017). It has been said that factors in young blood plasma start neural differentiation, increase the number of synapses and N-methyl-D-aspartate (NMDA) receptors in dendrites, which are also linked to learning and memory, and increase branching and spine-like formations (Gan and Südhof, 2019). In the measurements made with immunostaining, it was determined that there was a decrease in neurogenesis in the dentate gyrus of the young parabiont and an increase in neurogenesis in the aged parabiont. This has shown that important central processes in the connected circulatory system can be induced bidirectionally (Villeda et al., 2011). In another recently completed study, young plasma was reported to reduce Alzheimer's disease-like brain pathologies and improve cognitive impairment in 3xTg-AD mice (Zhao et al., 2020). However, in this study, it was not seen that there was a significant difference in anxious behavior in old rats after young plasma transfer.

The aged rats used in the study were 24 months old and were 25 months old after one month of plasma administration. This period corresponds to 60-70 years of age with human age. For rats, the 5-week period is counted as 7-8 years of age in human life (Sengupta, 2013). During the test, it was seen that the old rats could not volunteer much in terms of researching the test apparatus due to their size and age. It is thought that this may keep older rats from showing the full effects of young plasma transfer on anxious behavior.

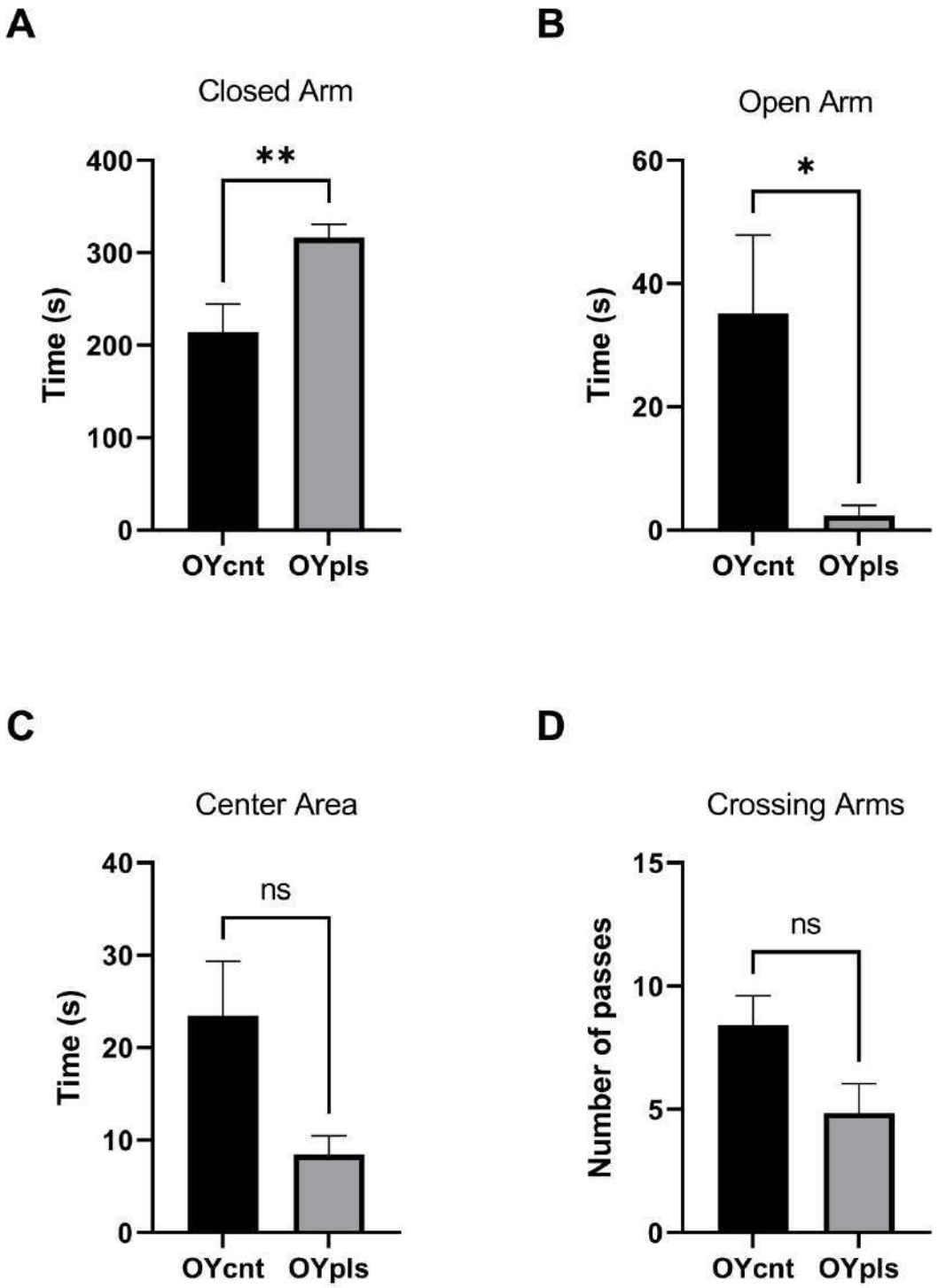

Figure 2: Statistical comparison of the time spent by young rats in the plus maze test apparatus after old plasma transfer: closed arm (A), open arm (B), center (C), and number of passes between closed arms (D)

The effects of aged plasma factors on anxious behavior in young rats were more pronounced, as the young rats used in this study were 5 weeks old and were able to explore the test apparatus very actively. The results obtained show parallelism with the effects of aged plasma in young

individuals in previously completed studies. The profound effects of aged blood in the young brain were observed in later studies, and it has been reported to cause significant reductions in neurogenesis in the sub-ventricular region (Rebo et al., 2016). It was observed that the performance of young mice to which aged plasma was transferred decreased in the radial arm water maze (RAWM), while the performance of aged mice to which young plasma was transferred increased in new object recognition behavioral tests with RAWM, contextual fear conditioning, and learning (Khrimian et al., 2017; Villeda et al., 2014, 2011). Similar results were obtained in the Barnes maze test (Castellano et al., 2017). The fact that old plasma factors have such a bad effect on the behavior of even 5-week-old rats shows both how important plasma factors are to quality of life and how damaging the aging process is to plasma factors.

V. CONCLUSION

In this study, the effects of plasma exchange between young and old rats on anxious behavior were studied. It was observed that there was no significant difference in young plasma factors in old rats compared to the control. However, we think that this result needs to be repeated because the size of the old rats and the fact that they were quite old caused difficulties during the test. On the other hand, old plasma factors were found to cause significant anxiety-like behavior in young rats. Because young rats are more mobile and more comfortable investigating the test apparatus, this makes this result safer. This strong effect of old plasma factors on behavior also shows that the importance of young plasma applications should be better understood.

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Contributions of the Authors

The authors contributed equally to the study

Conflict of Interest Statement

There is no conflict of interest between the authors.

Statement of Research and Publication Ethics

The study is complied with research and publication ethics.

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A Study on the Phytochemical Composition and Potential Benefits of *Syzygium Guineense* Wild (Guineense): An Overview

Feudjio Alfrodite Flore, Nganmou Ngongang Beactrice, Tankeu Nzufo Francine, Kemnoe sebatien, Tepa NJIJIEP Arnaud Gabin, Biapa Nya proper Cabral & Pieme Constant Anatole

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ABSTRACT

Syzygium guineense is one of the most widespread African tree species about more than 30 m tall with edible fruits.

Aim: Present review is an attempt to provide utmost information based on ethnomedicinal, phytochemical and pharmacological aspects of S. guineense.

Method: We searched PubMed, Medline, EMBASE, CINAHL, Psyc INFO and Web of Science databases to identify studies reporting phytochemical and pharmacological aspects of S. guineense. We made a systematic review of all the activities that have already been done on S. guineense.

Keywords: systematic review, syzygium guineense, phytochemical, pharmacological activity.

Classification: DDC Code: 577.314 LCC Code: QH343.7

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Results: A total of one hundred and seventy-eight articles were downloaded, sixty-six studies were included. Primary constituent's chlorophyll, lipids, sugars and proteins while secondary compounds include alkaloids, terpenoids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin. Research also has shown that S. guineense powder contains minerals such as Calcium, Potassium, Rubidium, Phosphorus, Strontium, Sulphur, Zirconium, Manganese, Iron, Titanium. Anti-inflammatory, analgesic, antioxidant, anti-diabetic, anti-cancer, anti-mycobacterial, anti-Sickle, antispasmodic, immunological and mollucidal activities were found.

Conclusion: This systematic review dealt with the phytochemical of S. guineense and its pharmacological activities. It emerges that S. guineense contains a variety of primary (amino acids, proteins, sugars) and secondary (polyphenols, flavonoids, saponins, tannins, alkaloids, terpernoids and many others) metabolites which contain several pharma-cological activities which act at different levels against oxidative stress, sickle cell disease, bacterial and viral infections.

Keywords: systematic review, *syzygium guineense,* phytochemical, pharmacological activity.

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I. BACKGROUND

Syzygium guineense (Willd) DC. is a tree of 10 to 15 m high, with a thick and tortuous bole, generally low branching, with a fairly dense crown and drooping branches [1]. It is a genus of flowering plants that belongs to the Myrtle family or Myrtaceae. The genus understand about 1100 species, and has a native range that extends from Africa and Madagascar through southern Asia [2, 3]. Many species are very poorly known and many more have not been described taxonomically. It's from 1996 that the articles on S.guineense have been found and this until 2021[4, 5]. Several are grown as ornamental plants for their attractive glossy foliage, and a few produce edible fruits that are eaten fresh or used in jams and jellies (6,7). Of

the different existing species, S. aromaticum (Clove) is one of the most commonly used like spices in kitchens, due to their potency as a chemopreventive agent and ability to treat several ailments [8]. The specie, S.guineense has been the subject of very few studies, hence the interest in taking stock of the work published on this subject.

Indeed, S. guineense is one of the most widespread African tree species about more than 20 m tall with a larger variety of growth forms like any other african plant [9]. Several synonyms are reported for this plant, such as Calyptranthes guineensis (Willd.), Calypthranthes guineense (Willd), Eugenia fourcadei (Dummer), Eugenia guineensis (Willd.) Baill. ex Laness., Syzygium fourcadei (Dummer) Burtt Davy and Syzygium fl euryi A. Chev, but no references to chemistry or biological activity have been found for these synonym names [10]. S. guineense is commonly known as "water berry" in English and its name differs depending on the locality or the region where the plant is found [11].

Different parts of plant, such as roots, leaves, bark and fruits are commonly used in traditional medicine as remedy for various ill health conditions due to its composition and its medicinal properties [12]. It has proven also to be a reservoir of phytochemicals compounds with pharmacological activities [13-19, 4, 5]. The aim of this review is to document utmost information on ethnomedicinal, phytochemical and pharmacological aspects of S. guineense.

II. METHOD

We searched Medline, Embase, Cinahl, PsycInfo, and web of Science databases to identify qualitative studies reporting *Syzygium guineense* views and experiences of carring for phytochemical composition and potentiel benefits. Key analytical themes were identified using thematic synthesis. The databases search was conducted from 1996 to 2021. This approach involves a systematic search of relevant litterature, quality appraisal of the included studies. Our reporting follows the guidelines for Enhancing Transparency of Reporting the Synthesis of Qualitative Research (ENTREQ) and Preferred Reporting Items for Systematic Reviews and MetaAnalyses (PRISMA). Data extraction was done according to two criteria: inclusion and exclusion. The articles included were all those dealing with S. guineense. All S. guineense related articles dealing with the phytochemistry and pharmacological activity of S. guineense.

Similarly, articles about S. guineense but not written in English or French, article with incomplete information about S. guineense and duplicate articles were excluded.

III. RESULTS

The search identified 182 unique records. Of these, 40 papers were excluded because they were duplicated. Of, the remaining 142, 12 papers were also excluded due to other language different from english and french. The remaining 130 studies led to the exclusion of 60 papers that did not meet eligibility criteria and due to incomplete information. This resulted in 70 studies being included in the synthesis.

Country, year of publication and the United Nations Statistics Division (UNSD) region of S. guineense

S. guineense is a fragrant species native to the wooded savannas and tropical forests of Africa. It is a water loving plant which grows to a height of 8 - 30 meters. In Africa and in southern Asia the plant is distributed in many country as well shown in fig.1. We note that Ethiopia is the country that published the most articles (19), followed by Cameroon (10). The United Nations Statistics Division (UNSD) region where this plant is located is indicated in fig. 2. Central Africa, East Africa and West Africa are the regions where research on *S. guineense* has been done the most.

The years of publication of *Syzygium Guineense* (Fig. 3.) vary between 1996 to 2021. We noted that from 2016 to 2021 the studies made on *Syzygium Guineense* had increased exponentially (55 %) followed by the years 2011 to 2015 (19%).

From 1996 to 2005 and from 2006 to 2010 we see that there was almost the same number of publications (14 %) *[20-30, 7]*.

Season, harvest time and parts of the plant used

Fig. 4a and b represent the different parts of the plant used during the studies. We found that most of the studies associate several parts for the same study. The leaves (22%), bark (6%) and fruits (7%) are the most used (Fig. 4a). In general, they use all the parts (25%) of the plant when they want to associate its (Fig. 4b). The activity of a plant is conditioned by the season (Fig. 5) and the time (Fig. 6) at which it is harvested. Also, the plant is harvested mostly in the dry season (36%).

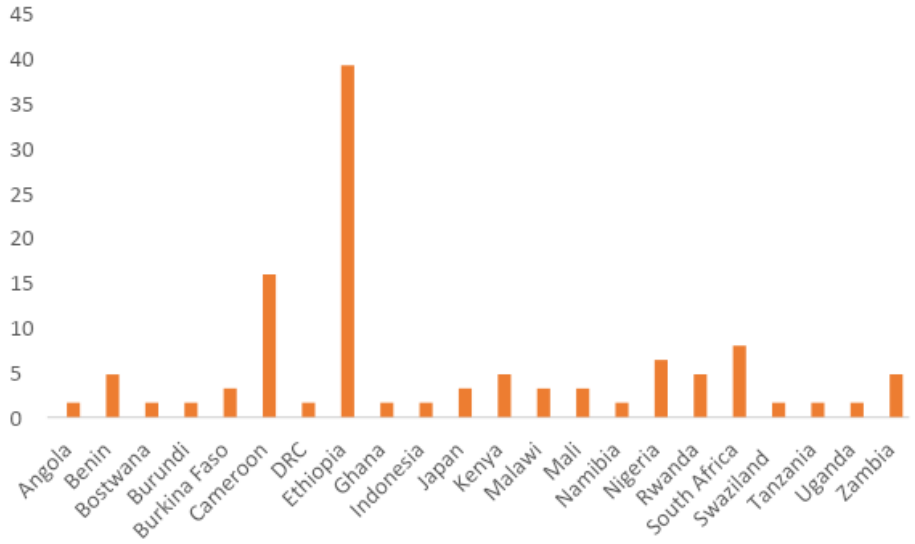

Fig. 1: Country where S. guineense is found

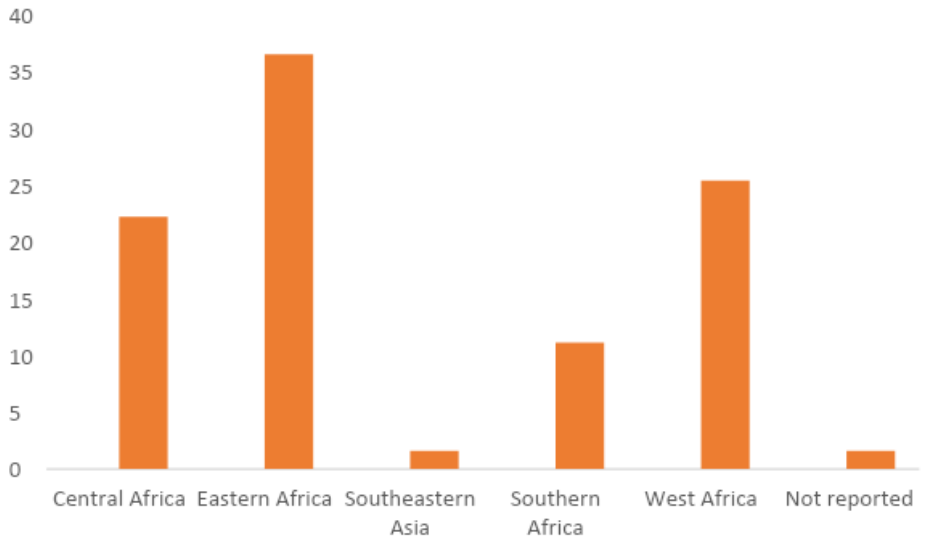

Fig. 2: United Nations Statistics Division(UNSD) Region

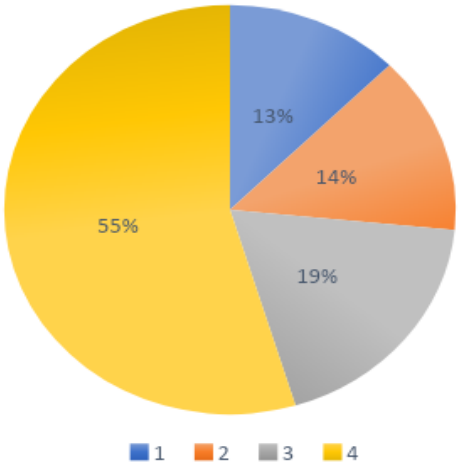

Fig. 3: Years of publication

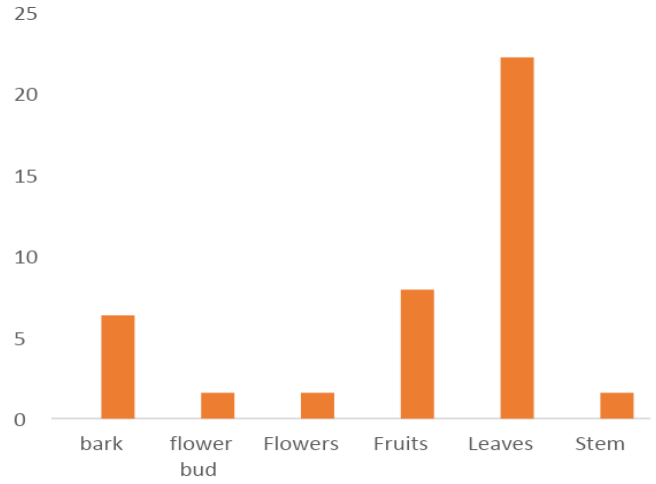

Fig. 4a: Part of the plant used

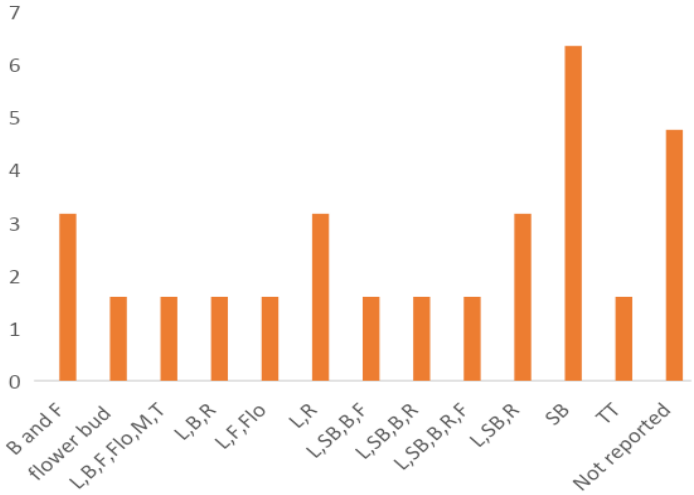

Fig.4b: Combined part of the plant used together B: Bark F: Fruits Flo: Flowers L: Leaves M: Marrow R: Roots SB: Stem bark TT: Tree trunk

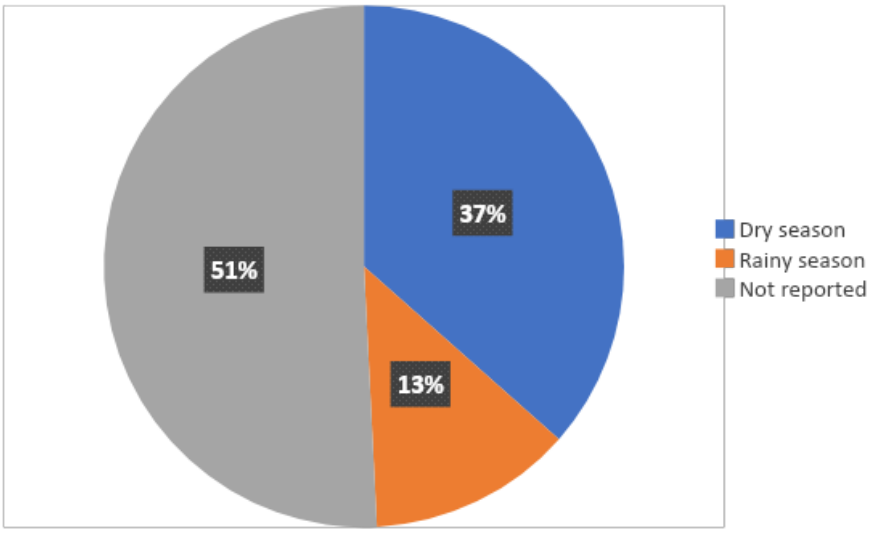

Fig. 5: Season of harvest

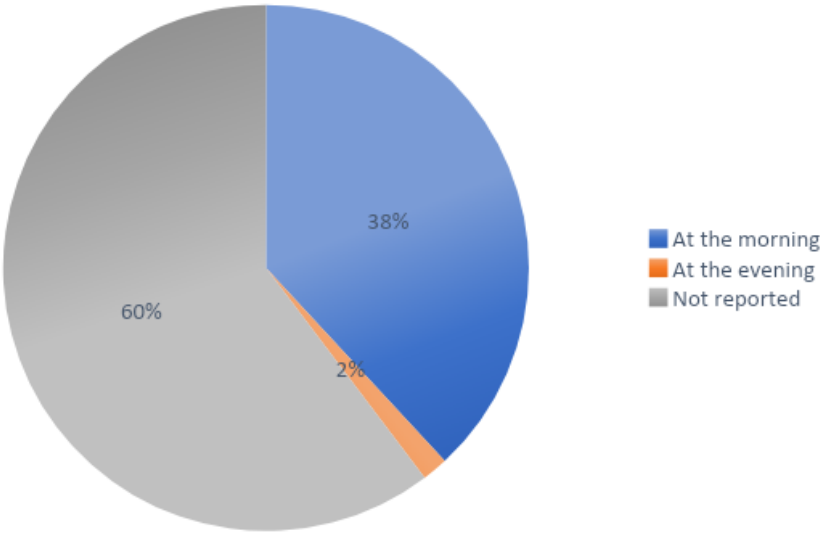

Fig. 6: Harvest time

Isolation method, Type of solvent and Polarity

Fig. 7. represents the different techniques used to isolate the different secondary metabolites. Solvent increasing polarity in turn coupled with Column Chromatography is the most widely used technique (23%). The solvents most used during isolation are polar (49%) (Fig. 8). Among these the most used are water (33%), methanol (9%) and the water-ethanol mixture (6%) (Fig. 9).

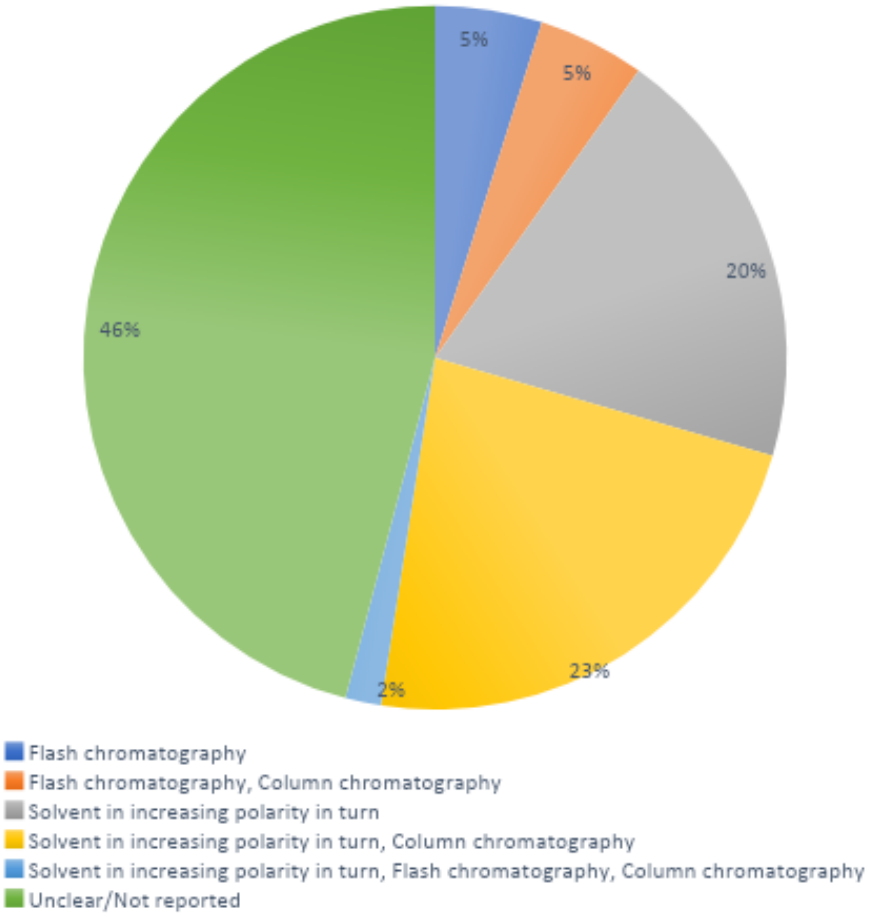

Fig. 7: Isolation methods

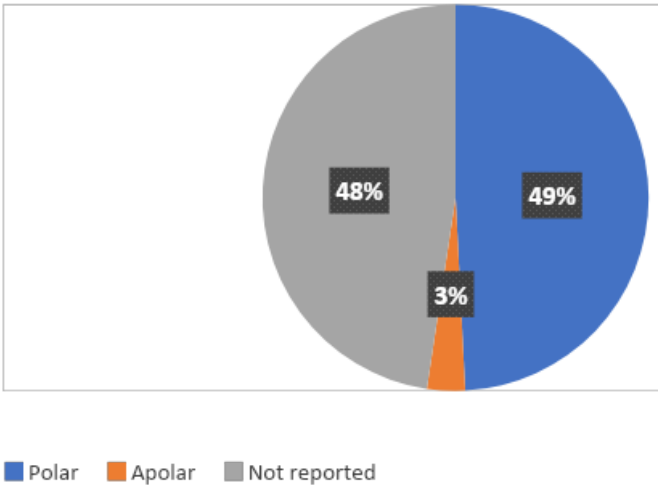

Fig. 8: Polarity of solvent

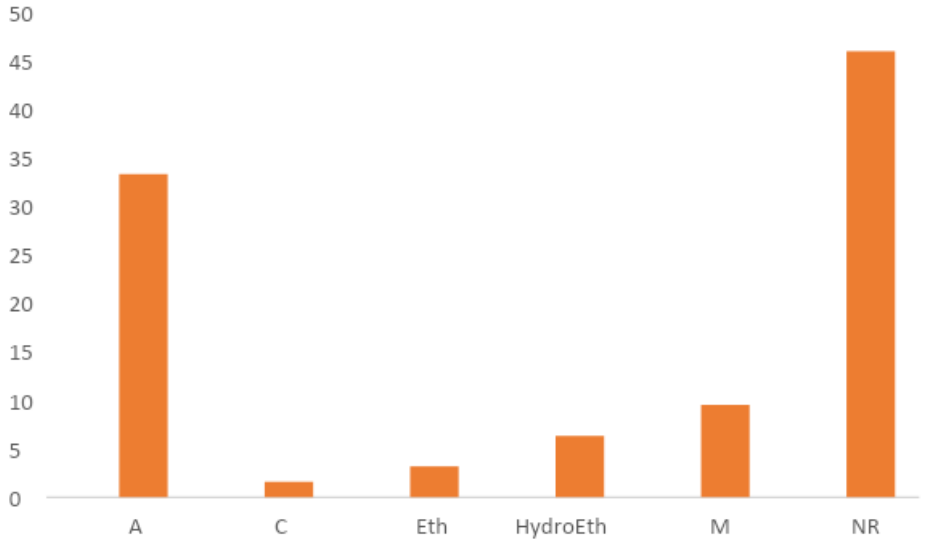

Fig. 9: Type of solvents used

A Aqueous .C Chloroform .Eth Ethanolic .Hydro Eth Hydroethanolic .M Methanolic .NR Not Reported

Vernacular name and Traditional uses of S. guineense

Vernacular name

Table 1 presents the different vernacular names used in Africa, particularly in Cameroon and Nigeria. We note that in Cameroon there are 5 appellations and this according to the localities while in Nigeria we have two appellations.

Table 1: Vernacular names of *Syzygium guineense*

Country	Dialect	Vernacular names	References
Nigeria	Afizere / Jarawa	"Afour"	[31]
Nigeria	Yoruba	"Ori"	[32]
Nigeria	Hausa	"Malmoo"	[33]
Nigeria	Yoruba	'' Adere"	[33]
Mali	Bambara	Kuri, Konyume	[34]
Mali	Bambara, Malinke	''Kokisa"	[35]
Mali	(Minyanka)	''Dugutaga"	[34]
Mali	Senoufo)	''Sukomon"	[34]
Mali	(Bobo-fing),	''dîbî ''	[34]
Mali	Dogon	''Alukile"	[34]
Congo	Kinande	''Omutusu"	[15]
Cameroon	Bangangté	"Tchankwop" and "Kakout"	[36]
Cameroon	Baya	"Zomoli"	[37]
Cameroon	Foufouldé,	"Asourahi"	[37]
Cameroon	Mboum (Foulbé)	"Asora"	[37]
Ethiopa	Amharic	"Dokima"	[38]
Ethiopa	Afaan Oromoo	"Baddessaa"	[38]
Ethiopa	English	"water berry"	[38]
South Africa	Guinea	"Waterpear"	[9]

Traditional uses of S. guineense

Table 2 presents the traditional use of *Syzygium guineense*. We find that the bark and the leaves are the parts most used to treat various ailments, in particular: malaria, diarrhea, epilepsy, asthma, cough, and even to treat wounds. *Syzygium guineense* also used as food and for construction.

Table 2: Traditional uses of *S. guineense*

Traditional Uses	Références
An infusion of the roots is used in African medicine to bathe a patient	[9]
An infusion of bark and roots soaked in hot water is used as a purgative.	[9]
In Mali to treat dermatosis, infertility, malaria, fever	[12]
In Nigeria for the amenorrhea and insanity	[39]
In West Africa, a decoction of leaves have been used in the traditional medicine for the treatment of wounds, ulcers, diarrhoea, rheumatism, and infections in Mali	[3, 40]
The leaves are used against hookworm and amenorrhea in Cameroon	[14]
In Cameroon 50 % is used in food, 15 % as energy source, 20 % in traditional medicine	[41]
Against stomach ache and ringworm, and in the treatment of wounds	[42]
Epilepsy, stomach-ache, diarrhoea, malaria, coughs, broken bones, wounds, asthma, sore throat, intercostal pain and as a tonic	[43]
In Ethiopia, leaf decoction of S. guineense is being used traditionally to treat malaria	[15]
Malnutrition, nasopharyngeal infections, pain, pulmonary disorders	[44]
For treating menstrual cycle disorder	[45]
A febrifuge and anti-abortifacient medication	[12]
Constipation, diarrhea, dysentery	[19]
Asthma, wound	[46, 47]
Arthritis, rheumatism, venereal diseases, malaria	[15]
Used against malaria, useful for the prevention and cure of malaria, and demonstrated antiplasmodial	[48]

Phytochemistry of S. guineense

Table 3 presents a summary of phytochemical compounds of the recorded in many studies. It is noted that the powders of *S. guineense* are rich in minerals such as: Calcium, phosphorus, iron, zinc, copper, magnesium, manganese, potassium. *Syzygium guineense* extracts are rich mainly in polyphenols, flavonoids, flavonones, tannins, saponins, alkaloids and many others.

Table 3: Phytochemistry of *S. guineense*

Types of compounds	Parts of plant used	Type of solvents	Major phytochemical compounds	References
minerals	fruit	Not need	aluminium (Al), calcium (Ca), iron (Fe), potassium (K), magnesium (Mg), manganese (Mn), phosphorus (P), lead (Pb), selenium (Se) and zinc (Zn).	[49]
	fruit	Not need	Calcium, Potassium, phosphorus, potassium, sodium, zinc and copper	[50]
	fruit	chloroform, ethyl acetate, n-butanol, and water	anthocyanin, carotene, chlorophyll	[51]
minerals	minerals in dried fruit pulp	Not need	Calcium (20,477 mg/100g), Potassium (443 mg/100g), Rubidium (3.2 mg/100g), phosphorus (8392 mg/100g), Strontium (60.5 mg/100g), Sulphur (1660 mg/100g), Zirconium (18.2 mg/100g), Manganese (8.5 mg/100g), Iron (268.3 mg/100g), Titanium (39.1 mg/100g).	[52]

Primary and secondary compounds	leaves, barks and roots	aqueous, hydroethanolic and methanolic extracts	sugars, proteins, lipids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin	[45, 54, 40,31, 14, 52, 48, 2]
Secondary compounds	fresh leaves	50.1% acetone, 33.5% butanol, 3.9%, 2.9% MeOH	Tannins	[55]
Primary and secondary compounds	dried leaves	essential oil	caryophyllene oxide (7%), δ-cadinene (7.5%), viridiflorol (7.5%), epi-α-cadinol (9.8%), α-cadinol (12.7%), cis-calamenen-10-ol (14%), citronellyl pentanoate (15.2%), β-caryophyllene (20.1%) and α-humulene (39.5%).	[56]
10 triterpenes	leaves	dichloromethane (CH_2Cl_2)/methanol (MeOH)	Namely, betulinic acid 1, oleanolic acid 2, a mixture of 2-hydroxyoleanolic acid 3a and 2-hydroxyursolic acid 3b, arjunolic acid 4a, asiatic acid 4b, a mixture of terminolic acid 5a and 6-hydroxyasiatic acid 5b, and a mixture of arjunolic acid 28--glucopyranosyl ester 6a and asiatic acid 28-glucopyranosyl ester 6b.	[40]
Primary and secondary compounds	leaves	ethanol extract	Phenolics like catechins and epigallocatechin-3-gallate elicit. Betulinic acid, oleanolic acid and ursolic acid	[57]
Primary and secondary compounds	leaves		Arabinogalactan polysaccharide	[16]
Primary and secondary compounds	leaves	methanol extract	Ten new polyphenols: flonoacetoides gallocatechin, myricetin, myricetin-3-Oglucoside, myricetin-3-O-rhamnoside, myricetin-3-O-glucuronide, myricetin-3-Oß-D-(6″l) galactoside, the gallotannins 1,2,3,6-tetra-O-galloyl ß-D-glucose and 1,2,3,4,6-penta-Olß-D-glucose, ellagitannins casuarictin and casuarinin.	[12]
Primary and secondary compounds	leaves	Hexane	terpenes/terpenoids (0.38%), hydrocarbons (42.1%) and the major compounds was organic acids (42.48%). Twelve (12) news phytochemical constituents were also identified: 4-dimethyl-7- (1-methylethenyl) azulene (2.06%), myristic acid (2.11%), Ylangene (2.42%), decahydro- 4 amethyl -1 - methylene - 7 - (1-methylethynyl)-naphthalene (γ-muurolone) (2.47%), 1-ethyl-2-methylbenzene (2.61%), 1,2-benzenedicarboxylic acid (2.71%), caryophyllene oxide (3.86%), pentatriacontane (3.95%), tetratriacontane (6.70%), n-hexadecenoic acid (11.94%), 9-octadecanoic acid (25.72%) and tetratriacontane (31.45%).	[2]
Primary and secondary compounds		Essential oil	92.63% of the essential oil constituents. Sesquiterpenoids (73.15%) and monoterpenoids (14.17%) were the main classes of the essential oil. Aromadendrene (6.98%), germacrene B (5.52%) and β-selinene (3.94%) were the predominant sesquiterpene hydrocarbons. The oxygenated sesquiterpenes were α-cadinol (6.68%), τ-cadinol (6.64%) and caryophyllene oxide (5.44%).	[56]

Primary and secondary compounds	stem bark extracts	dichloromethane extract	β-sitosterol and Betulinic acid on the basis of spectroscopic	[58]
Ellagic acid	stem bark	Methanolic extract	3-O-Methylellagic acid-4'-O-α-rhamnopyranoside. 3-O-Methylellagic acid-4'-O-α-2"-O-acetylrhamnopyranoside 3-O-Methylellagic acid-4'-O-α-3"-O-acetylrhamnopyranoside	[40]

Pharmacological activities of S. guineense

Antiinflammatory, Analgesic and Immunological activities of S. guineense

Anti-inflammatory and analgesic activities of the ethanolic extract of the leaves of *S. guineense* was investigated in rats and mice by *[31]*. They showed that at concentrations of 500 mg/kg and 1000 mg/kg the extract was found to possess significant ($P<0.05$) analgesic effects on the hot plate model, but only the concentration of 1000 mg/kg possessed significant ($P<0.05$) anti- inflammatory and analgesic effects on the writhing test. According to *Turner*hot plate test is a model for assaying effects of drugs on central pain. Drugs that are effective in this model have central analgesic effect. *[53]* showed that aqueous decoction of the leaves of *S. guineense* of Malian have anti-inflammatory activities at doses of 100 mg/kg and 200 mg/kg. *[16]* have isolated and characterised two immunologically active polysaccharide fractions from the leaves of *S. guineense*. One of the fractions contained an arabinogalactan type II polysaccharide, while the other polysaccharide fraction was a mixture of oligosaccharides of the pectic type. He showed that both polysaccharides had high complement fixing ability, as well as the ability to stimulate nitric oxide release from macrophages, up-regulation of CD86 on dendritic cells, and proliferation of B cells. These arabinogalactan polysaccharides potently stimulated the secretion of proinflammatory and anti-inflammatory cytokines from both B cells and dendritic cells.

Antioxidant activities of S. guineense

S. guineense provides a rich source of antioxidant compound that act as scavengers of the oxygen atom or free radicals in the body *[14]*. Differents parts of this plant have been the subject of several studies aimed to show that extracts of *S.guineense* were able to scavenge DPPH, nitric oxide (NO ●), hydroxyle, and ABTS + free radicals. In addition, *S. guineense* crude extracts of barks inhibited the oxidative ferric chloride induced damage in liver homogenates by increasing the antioxidant enzymes SOD, catalase and peroxidases and the hydro-ethanol extract of leaves exhibited the highest inhibitory effects on lipid peroxidation *[14]*. *[57]* was observed an antioxidant effect produced by methanol extract of *S. guineense* leaves in rats in a concentration-dependent manner. In facta maximum radical scavenging effect was produced at a concentration of 1.25 mg/mL of extract and a concentration of 0.2 mg/ml was estimated to be the efficient concentration required to elicit 50 % radical scavenging capacity.

Similarly, other study showed that extracts both from leaves and bark of *S. guineense* inhibited the oxidative damage mainly in liver and brain homogenates *[59]*. In this study, three extracts (aqueous, ethanol and hydro-ethanol) from the bark of *S. guineense* were used to determine the free radical scavenging and antioxidant potential of the extracts. They have shown that all the extracts exhibited a free radical scavenging potential in a concentration dependent manner which varied from 15.18 ± 0.80 to 97.15 ± 0.71% depending to the type of extract and the method used. However, the ethanol extract had the higher total antioxidant capacity. In fact, these results have shown that these extracts are rich in hydrogen atom and or electron donating-substances as phenolic derived compounds, glycosylated derived compounds and anthocyans capable of pairing with the unstable DPPHo radical. In parallel, all the extracts lowered significantly ($p<0.05$) the level of MDA when compared to the negative control. However, the

aqueous- ethanolic extract exhibited the best protective activity by lowering the MDA content in the liver, kidney and brain homogenates comparatively to the negative control *[59]*.

Antidiabetic potentials and organoprotective effect of S. guineense

[57] examines the effects of a methanol extract of *Syzygium guineense* leaves in streptozotocin (STZ) induced diabetes in rats. These effects were evaluated on the activity of the enzyme alpha glucosidase and the 2,2-diphenyl-1-picrylhydr azyle radical. The results showed that the extract have an antihyperglycemic action probably due to its ability to inhibit alpha glucosidase, scavenge free radicals, and increase the absorption and storage of intrahepatic glucose. This extract produced dose-dependent decrease in blood sugar in diabetic rats in an oral glucose tolerance test after diabetes injection and a maximum dose of 1000 mg/kg of extract. A dose of 250 mg/kg of extract significantly (P<0.01, 0.001) decreased the hyperglycemic peak in diabetic rats and was comparable with metformin, the group of diabetic control.

Similarly in this study after 14 days of experiment, serum biochemical analysis showed that the extract did not significantly change the electrolyte and urea levels however they noted a decrease in serum levels of liver marker enzymes, total and direct bilirubin albumin and creatinine; dose-dependent compared to the diabetic control ***[57]***. Also at the dose 250 mg / kg extract reduced significantly (P<0.05) serum cholesterol, triglycerides and high density lipoprotein (HDL) in a non-dose dependent manner. They also noted that at doses 250 and 500 mg / kg, extract showed reversal of glomerular damage compared with the diabetic untreated group.

[59] was assessed the protective effect of barks extracts of *S. guineense* against ferric nitrilo-acetate-induced stress in the liver, heart kidney and brain tissues of *wistar* rat homogenates. Their results show that Fe3+- NTA led to a significant increase of lipid peroxidation associated with SOD, catalase, and glutathione peroxidase activity depletion in all tissues assayed compared to the negative control. These results demonstrated important organo protective effect on all the tested homogenates by delaying or preventing lipid peroxidation and restoring enzymatic and non enzymatic markers activities.

Antihypertensive and vasodepressor Activities of S. guineense

A study in Tanzania on the methanolic extract of the bark of *S. guineense* in rats showed that this extract produced prolonged hypotension in anaesthetized rats. A dose of 5 µg lowered systolic, diastolic and mean blood pressure by 16%, 22% and 17%, respectively, below the pre-drug levels.

The Maximum effect was obtained at a dose of 40 µg when the systolic, diastolic and mean blood pressures fell by 23%, 36% and 28%, respectively, below the pre-drug levels ***[43]***.

The evaluation of the antihypertensive activity of the hydroalcohol extract of the leaves of *S. guineense* in an animal model in 2010 in Ethiopia by Ayele, *and al* showed that the extract had an antihypertensive effect most likely caused by dilation of the blood vessels. In fact, after three days of oral administration of the different single doses 50, 100 and 150 mg /kg, the extract reduced blood pressure in a dose and time dependent.

More precisely, the extract caused an overall reduction (p <0.05) in systolic blood pressure of 6.9, 34.0 and 40.8 mmHg, respectively. However, diastolic blood pressure was significantly reduced (p <0.05) by 100 mg / kg (10.3 mmHg) and 150 mg / kg (18.4 mmHg) *[60]*.

Concerning its vasorelaxant effect on isolated aorta, the extract caused a dose-dependent relaxation of aorta precontracted with KCl at a concentration of 5–70 mg/mL, with a maximum relaxation of 56.22% achieved at 70 mg/mL concentration. However, this study indicated that the vasorelaxation of the extract does not involve cholinergic receptors as well as ATP dependent K+ channels or NO/cGMP pathway since blocking them with atropine did not augment the effect ***[60]***.

Anti-Sickle and Anti-venom proprieties of S. guineense

Sickle cell anemia is also one of the diseases traditionally treated by the use of *S. guineense* ***[54]***. In 2007, Kisangau*and al* conducted a study which consisted of isolate and characterize anti-drepanocytosic compounds from five medicinal plants including *S. guineense* from the DRC and South Africa. The chromatographic methods used made it possible to isolate and purify the compounds and to test their anti-sickle cell activities using the Emmel test. Different extraction was carried out on *S guineense* leaves using organic solvents: hexane, dichloromethane, ethyl acetate, methanol and 80% aqueous methanol. betulinic acid, betulinic acid acetate and maslinic acid isolated from hexane extracts, dichloromethane and ethyl acetate of *Syzygiumguineense* of DRC, showed high antisickling activities at more than 70% of normalization ***[19]***.

The hot methanolic extract of *Syzygium guineense* has been claimed to have antivenom properties against Najakatiensis venom in rats ***[39]***. Indeed the potential of neutralization of the venom in the rats was studied by the measurement of the glycemia, the lipid profile, the activity of creatine kinase, the pulse. The measurement of these parameters in plasma is important for the evaluation of the pathophysiological state of snakebite victims. The results showed that the venom of Najakatiensis can disturb the metabolism of the rat and the plant extract was able to neutralize the lethality induced by the venom ***[39]***. More specifically these results have shown a reduction ($P < 0.05$) in the pulse rate, in hyperglycemia induced by the snake venom, in rectal temperature of the extract treated groups following envenomation, when compared with group controle. Likewise the results showed reduced significantly ($P<0.05$) Creatine Kinase Activity, and neutralization the edema formation induced by Najakatiensis venom. In this study, the plant extracts offered some protection against the lipolytic activity of the venom ***[39]***.

Mollucidal, Antispasmodic, and Antidiarrheal activities of S. guineense in animal model

The ethanolic extracts of stem bark of *Syzygium guineense* showed molluscicidal activity ***[61]***. The aqueous and 80% methanolic extract of the leaves tips (twigs), stem barks and unripe and ripe fruits of *S. guineense* in Ethiopia showed antispasmodic activities on of guinea pig *in vitro* and *in vivo* in the small intestine transit ***[45]***. In fact, on Guinea pig ileum *in vitro* experiments, twig aqueous extracts of *S. guineense* showed more inhibition of Acetylcholine and histamine induced contractions of the tissues than any of the other extracts. The inhibitory activities of all extracts except fruit aqueous and Fruit 80% methanolic extracts were also significant in a dose dependent manner from 50 - 200 µg/ml. These results show the spasmolytic properties of the extracts. Similar results were reported for the plant by ***[42]***. where he methanolic extract of stem barks of *S. guineense*(collected in Tanzania) inhibited intrinsic contractions in isolated ileum tissue of rabbit. The inhibition, at bath concentrations of 0.5-2.0 mg/ml, was dose-related but non-linear. Both the aqueous and hydroalcoholic twig and stem bark extracts of *S. guineense* had spasmolytic effect on Guinea pig ileum, while, its fruit extract showed spasmogenic effect at lower dose and no effect at higher doses in both Acetylcholine and Histamine induced contraction.

In the in vitro experiment, leaf tips aqueous and Twigs 80% methanolic extracts at concentration of 100 and 200 µg/ml were found to have comparable antispasmodic effect as that of atropine and dexchlorpheniramine ***[45]***.

The Antidiarrhoeal activity was also determined ***[45]***. In the antidiarrheal study, the aqueous and 80% methanolic crude extracts of *S. guineense* given orally, exhibited significant inhibitory dose-dependent activity against castor oil-induced diarrhea at all doses (50, 100 and 200 mg/kg). It has been found that antidiarrhoeal activity can be associated with the antimicrobial activity of leaf and bark extracts of *S. guineense* which was reported to have potent antibacterial effect against diarrhea caused by bacteria ***[4, 40]***

Antiparasitic activity of S. guineense

S.guineense has also been studied for its effects against parasites. Thus, the antimalarial effect of its leaf extract has been evaluated in rodent models in Ethiopia ***[48]***. The results of *in vivo* antimalarial activity test showed that the crude leaf extract of *S. guineense* exhibited considerable suppression ($p < 0.05$) of the parasite at doses of 600 and 400 mg / kg with a chemosuppressive value of 59.39% and 49.09% respectively. This reduction of the parasitaemia level is dose-dependent at all tested doses. In addition to these results, average chemosuppression at the highest dose used in the study (600 mg/kg body weight), was 48.57% which is lower than that exhibited by the Chloroquine, the standard drug (72.85%) which confirmed the efficacy of *S. guineense* supporting its traditional use against malaria ***[48]***.

Furthermore, ***[52]*** showed that the ethanolic extract of *S. guineense*have antihelmintic activity in a dose dependent manner giving shorter time of paralysis and death compared to the Albendazole tablets. In fact, the evaluation of anthelmintic activity was based on the time necessary to cause 100% paralysis and 100% death. In all cases tested, the crude ethanolic extract of S. guineense required more time to cause paralysis and death than albendazole. At lower concentrations (50 mg / ml and 30 mg / ml of crude ethanolic extract), the time required to cause 100% death was slightly greater than 0.025% compared to the negative control. In addition, at the concentration of 100 mg / ml, the time required to obtain 100% death for the ethanolic extract of *S. guineense*was 6% higher than that of ***[52]***.

Anticancer activities of S. guineense

Others species belonging to the Syzygium genus have been well-studied for their anticancer properties. However, very few studies have been done on the anticancer effect of *S. guineense*. A study carried out by ***[13]*** on *in vitro* antiproliferative effect of *S. guineense* extracts showed that the ethanolic extract of leaves possessed the ability to inhibit the growth of both HPV 16+ (SiHa) and HPV18 + (HeLa) cervical cancer cells *in vitro* using the sulforhodamine B (SRB) method. Furthermore, the authors showed that cell cycle arrest and apoptosis induction might be the possible mechanism responsible for the observed cell growth inhibition.

Similarly, ***[62]*** studied the effect of tannins from some cameroonian plants, including *S. guineense* on Triple-negative breast cancer (TNBC) and colon cancer (CC). The results showed that extracts from *S. guineense* showed a clear inhibitory activity. In fact*S. guineense* inhibited Wnt-dependent transcription, taken at the concentration of 50 µg / ml, the extract of the plant completely inhibited the Wnt-dependent TopFlash transcription, but not the constitutive CMV-Renilla transcription. Thus, the active compound (s) from *S. Guineense* do not contained general transcription-suppressive effects, but specifically inhibit Wnt3a stimulated β-catenin-dependent transcription in the TNBC cells. Also, the autors showed that S. guineense extract have an ability to decrease basal levels of β-catenin induced by Wnt3a. In the BT-20 TNBC cell line and there was concluded that Tannins from *S. guineense* suppress Wntsignaling and proliferation of Wnt-dependent tumors through a direct effect on secreted Wnts.

Antibacterial activities of S. guineense

Scientifically, the different parts of *S. guineense* (leaves, root,bark, stem, and twigs) have shown proven efficacy against pathogens (bacteria and fungi) ***[63]***. The table 3 presents the different antibacterial activities already carried out on *S. guineense*.

Cytotoxicity activity of S. guineense

The safety of the extract of leaf when taken acutely was performed according to the OECD guideline 425. A fixed dose of 2000 mg/kg body weight of *S. guineense* leaf extract was administered to a single mouse via the oral route by gavage. The result showed that *S. guineense* leaf extract didn't cause death of the study mice at the limit dose of 2000 mg/kg. Similarly, both physical and behavioral observations of the study mice also did not point out any visible signs of toxicity. This indicates that the LD_{50} of the extract is above 2 000 mg/kg ***[48]***. The toxic effect of chronic

administration of the aqueous extract of *S. guineense* on the histopathology of the liver mice was investigate *[66]*. The oral LD_{50} of the aqueous extract was 14.1 mg/kg and the tissue samples were collected from the liver for examination. The results observed in this study showed that mice treated at a dose of 200 and 400 mg/kg showed no histopathological changes as compared to the control. However, tissue morphology of mice treated with 600 mg/kg of the extract showed hemorrhagic necrosis, and cytoplasmic vacuolations. Similarly, congestion of liver sinusoids was observed in mice treated with the extract *[66]*. Sub-chronic toxicity of ethanol leaf extract of *Syzygiumguineense*on the biochemical parameters and histopathology of liver and kidney in the rats was also investigated. This study shown that administration of *S. guineense*in rats at a dose of 1000 mg/kg body weight affected the food consumption, weight gain, and serum levels of liver and kidney enzymes suggesting that *S. guineense*intake at high doses may be toxic *[5]*.

Also the teratogenic effect of *S. guineense* had been evaluated by Melese*and al* in Ethiopia in 2021. That study concluded that, administration of the hydroethanolic extract of *S. guineense leaves* to the pregnant dams does not produce significant skeletal and soft tissue malformations in rat fetuses. The plant extract did not produce significant teratogenic effects on rat embryos/fetuses up to 500 mg/kg doses; however, as high dose (1000 mg/kg) of the plant extract reduced the growth of rat embryo. They also recommended that it is not advisable to take large doses of the plant during pregnancy *[5]*.

IV. DISCUSSION

S. guineense is a fragrant species native to the wooded savannas and tropical forests of Africa. In Africa, the plant is widespread in Ethiopia and Cameroon. This abundance may be due to the quality of the soil and the favorable climate in these countries *[2]*. In the eastern part of Africa, this plant is widely represented *[67]*. The number of studies on this plant has increased exponentially since 2016 to the present day. The results of our research number 66 articles that have worked on *S. guineense*.

In general, the most used parts of the plant are the leaves, the bark, the roots, and the fruits. The isolation of the secondary metabolites contained in this part is most often done using solvent increasing polarity in turn coupled with column chromatography *[48]*. During the isolation and extraction of bioactive compounds, the most commonly used solvents are, water, hydroethanolic solvent and methanol.

In this study we found that the plant was majority harvest in the morning time and at the dry season according to the two seasons we have. Botanists explain that in the morning most of the active principle is concentrated in the plant. On the other hand, in the evening, the plant is mainly concentrated in CO_2 *[68]*.

This review also found that according to the country and the locality this plant has many vernacular names. It'scommonly known as water berry in English *[11]*. In Nigeria this plant is known as "afour" in Afizere / Jarawa and "ori" in Yoruba *[32]*. In Cameroon it is called "Tchankwop" and "Kakout" in Bangangté, "Zomoli" in Baya, "Asourahi" in Foufouldé, "Asora" in Mboum (Foulbé) *[34, 36, 37]*.. We can find several names in the same country because each region has its own dialect *[33]*.

Another finding of this review shown that different part of *S. guineense* is traditionnaly used to treat many desease. In this study we observed that leaves, bark, and fruits were the most part of the plant used. In Nigeria the bark of *S. guineense*is used in traditional medicine to treat gastrointestinal disorders and also as a purgative *[69; 39]* and against diabetes joint together with leaves of Jatropha curcas*[70]*. In the Democratic Republic of Congo, the leaves are used against malaria *[15]*. Fruits are a valuable food for gorillas and chimpanzees and also consumed in flour and as condiments, spices, flavors.In Cameroon, the wood of *S. guineense* is used as fuel for the household, to construction and for carpentry. Twigs and leaves are used against hookworm and leaves against amenorrhea and madness. *S. guineense* sap yields a black dye used to color textiles *[36]*.

Morever, several studies carried out in various African countries such as Cameroon, Ethiopia, Mali, Nigeria, DRC, related to the phytochemical screening of aqueous, hydroethanolic and methanolic extracts of various parts of *S. guineense* such as leaves, bark and roots have already been done. These studies showed that all samples contain sugars, proteins, lipids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin.

furthermore, the level of polyphenol varied significantly ($p < 0.05$) between the different parts of the plant and between the solvents and indicated also that the bark has the highest level of polyphenols and that hydroethanolic extract was the best solvent *[40, 54, 14, 52, 48, 2]*.

Morever, several pharmacological activities are linked to the presence of these phytochemicals.

All of these pharmacological activities have already been discussed above.

V. CONCLUSION

The findings of this study contribute to an in-depth and valuable understanding of studies that have already been done on *Syzygiumguineense*. *Syzygiumguineense*is a plant endowed with pharmacological activities (anti-Sickle and Anti-venom, antioxidant, anti-inflammatory, antiparasitic, antidiabetic, antihypertensive, antispsmodic, antidiarrheal, antibacterial, anticancer, analgesic, and vasodepressor) directly related to its phytochemical composition (sugars, proteins, lipids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin). The most used parts are the leaves, the bark, the roots and the fruits. The plant is harvested most often in the dry season and very early in the morning.

Authors' contributions

All authors (FA, NB, KS, PC, and CA) contributed to the design of this review. FA and NB conducted the literature search, screening and quality assessment. KS extracted and coded the data, analysed the data withMedline, Embase, Cinahl, PsycInfo. FA drafted the initial and final manuscript. All authors (FA, NB, KS, PC, and CA) critically reviewed and approved the final manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Factors Contributing to Poor Biomedical Waste Management among Health Workers in Katabi Military Hospital in Entebbe District

Masagazi Edward

ABSTRACT

A descriptive cross-sectional study design was carried out from August 2021 to March 2022 to assess the factors contributing poor BMWM among health workers in Katabi Military Hospital. The study aimed at finding out the knowledge, practices and the effects of poor BMWM among health workers in Katabi Military hospital–Entebbe district and sample size of 50 respondents was determined using Kish and Leslie formula (1965). The study site was purposely selected because it was one of the areas having many staff we were targeting.

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Definitions

Biomedical wastes: This refers to any solid and or liquid waste including its container and any intermediate product which is generated during the diagnosis, treatment or immunization of human beings or animals or in research pertaining there to or in the production or testing thereof.

Biomedical waste management: This means the activities that are involved in handling wastes which include waste collection, segregation, storage, treatment, transport to final disposal site and final disposal.

Pharmaceutical wastes: It includes expired or unused pharmaceutical products spilled or contaminated pharmaceutical products, surplus drugs, vaccines or sera and many others.

Segregation of wastes: This refers to sorting and separation of waste types to facilitate recycling and correct onward disposal.

Pollution: Refers to the presence of harmful substances or poisonous substances in an environment.

Infectious wastes: Refers to waste contaminated with blood and other bodily fluids.

Factors: Refers to elements contributing to a particular result, situation.

ABSTRACT

A descriptive cross-sectional study design was carried out from August 2021 to March 2022 to assess the factors contributing poor BMWM among health workers in Katabi Military Hospital. The study aimed at finding out the knowledge, practices and the effects of poor BMWM among health workers in Katabi Military hospital–Entebbe district and sample size of 50 respondents was determined using Kish and Leslie formula (1965). The study site was purposely selected because it was one of the areas having many staff we were targeting.

Respondents were interviewed using pre-coded questionnaires designed in English and the collected data was analyzed using SPSS version 20.0 and later presented in form of tables, pie charts, graphs, and text statements.

Social-demographic characteristics of the study participants were: majority (50%) of the respondents were aged between 30-39 years, males were more than females by (66%), (40%) were single and (42%) of the respondent were nurses. Respondents had some knowledge about any discarded biological products such as used cotton swabs and blood from wards and laboratories being regarded as medical wastes, Practices of health workers about BMWM were; disposing all kinds of waste into a general bin, not segregating the biomedical waste according to different categories. There is need to institute deliberate interventions by Katabi hospital to provide community with clean dust bins and sanitation facilities to ensure safe disposal of fecal and solid waste, Government and other stake holders should ensure that the health workers receive trainings on how to manage biomedical wastes of any form and supplies to be used should be readily available and should be taught on how to use them i.e. personal protective equipment like gloves, aprons, masks etc. The district health service provider should intensify effective health education of the community, paying special attention to biomedical waste disposal management

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education and communication materials geared towards sensitizing them so as to reduce the incidence of pollutions and raising infections and DHO should work with and facilitate administrators, village health teams to promote good sanitary environment to reduce on the incidences of injuries from dumped sharp materials and infectious materials to both the staff and community at large.

I. CHAPTER ONE INTRODUCTION

This chapter briefly explains the background of the study, problem statement, study objectives, research questions, significance, justification and scope of the study.

1.1 Study Background

Biomedical waste refers to any waste that is generated during the diagnosis, testing, treatment, immunization of human beings or animals, in the research activities pertaining to their productions or testing (Mohit, 2017).

Health care institutions and various hospitals, diagnostic centers, blood banks, dental centers and research centers produce a variety of waste like dressing material, cotton pads, anatomical body parts, plastic disposal items, needles, drugs, chemicals, food items, intravenous tubing's, cannula and catheter (Annanthachari, 2016).

Waste management refers to managing waste by multiple techniques to achieve solid waste and resource conservation goals. The techniques may include waste reduction, re-use, re-cycling, composting, transformation, disposal to landfills and others.

Effective management of biomedical waste is a vital issue not only to hospitals, but also to the environment, law enforcement agency, media and to the general public (C, 2017). The purpose of BMWM is mainly to reduce waste generation, to ensure its efficient collection, handling, as well as safe disposal in such a way that it controls infection and improves safety for employees working in the system. For this, a conscious, coordinated and cooperative effort has to be made from physicians to ward boys (Chudasama, 2013).

The proper health care waste management include five steps namely segregation of biomedical waste at the point of generation, treatment, storage, transportation and final disposals. The segregation of biomedical waste at the source of generation is the first step, but crucial step in health care waste management (HCWM) because of specific methods needed for the treatment and disposal of different categories of waste. The health personnel who are involved in handling the biomedical waste at different point of generation in hospital include doctors, nurses, lab technicians, ward boy etc. Thus the knowledge regarding BMWM among health care personnel have greater impact on health and environment (Anish, 2013).

Globally, 18-64% of health care institutions are reported to have unsatisfactory BMWM facilities; predictors' lack of awareness, insufficient resources and poor disposal mechanism (WHO, 2013).

In Africa, healthcare waste (HCW) has not received the much needed attention that it deserves. This is because of the inadequate resources in these countries resulting into low priority for HCW management. In many countries, there is limited segregation of hazardous and medical wastes and usually mixed with non-infectious waste. Inadequate knowledge and attitude among the health care worker (Tsebeni, 2019).

In Uganda, during the evaluation of injection safety and BMWM, it was found out that 92% of waste handlers have poor waste disposal methods, 3.4% have acceptable waste disposal methods and 4.6% have good waste disposal methods (Muhwezi, 2014) and Katabi hospital is one of them.

1.2 Problem Statement

Globally, 18%-64% of health care institutions are reported to have unsatisfactory BMWM facilities; predictor's lack of awareness, insufficient resources and poor disposal mechanism (WHO, 2013).

One of the problems Uganda faces today is improper handling and disposal of biomedical wastes. During the evaluation of injection safety and BMWM in Uganda, it was found out that 92% of waste handlers have poor waste disposal methods, 3.4% have acceptable waste disposal methods and 4.6% have good waste disposal methods including Katabi military Hospital (Muhwezi et al, 2014)

Inadequate knowledge and unsatisfactory management practices among the health care workers are major challenges in the management of HCWs. Previous research indicates that HCWM may be affected by lack of formal training, lack of knowledge on HCWM, limited interest from hospital administration.

Biomedical wastes constitute a large portion of infectious wastes, which are potentially dangerous, because they may be resistant to treatment and possess high pathogenicity or ability to cause disease. Biomedical waste is also a source of contamination of land and water sources if not rendered harmless before its burial on land or disposal water. Furthermore, biomedical waste emits harmful gases, which leads to atmospheric pollution, when treated in open burning or burning in incinerators. The emissions can cause respiratory and skin diseases or even cancer, if precaution protocols are ignored.

Therefore, this study aims at assessing factors contributing to poor biomedical waste management among health workers in Katabi Military Hospital in Entebbe District.

1.3 Study objectives

1.3.1 General Objectives

To assess factors contributing to poor BMWM among health workers in Katabi Military Hospital in Entebbe District.

1.3.2 Specific Objective

To find out the health facility related factors contributing to poor BMWM among health workers in Katabi military hospital- Entebbe district.

To find out the individual-related factors contributing to poor BMWM among health workers in Katabi military hospital- Entebbe district.

To assess the effects of poor BMWM among health workers in Katabi military hospital– Entebbe district.

1.4 Research questions

What are the health facility related factors contributing to poor BMWM among health workers in Katabi military hospital– Entebbe district?

What are the individual related factors contributing to poor BMWM among health workers in Katabi military Hospital-Entebbe district?

What are the effects of poor BMWM among health workers in Katabi military hospital– Entebbe district?

1.5 Study Significance

This study provides detailed information about the health facility related factors, individual related factors contributing to poor BMWM and effects of poor BMWM among health workers.

Results of this study were helpful in bridging the knowledge gap about proper BMWM to the health workers, hospital administration, the public of Entebbe district and the country at large that are at risk of the impact of poor BMWM.

The study findings were used by the researcher to compile a research report in partial fulfillment for the award of diploma in pharmacy.

1.6 Study Scope

1.6.1 Content scope

The study aimed at determining the factors contributing to poor biomedical waste management among health workers in Katabi military hospital.

1.6.2 Geographical scope

The study was carried out in Katabi military hospital in Entebbe district in Entebbe UPDAF Air force base.

1.6.3 Time scope

The study was carried out between June 2021 and December 2021.

II. CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This section provides the background understanding of different research studies that have been carried out regarding to factors contributing to poor biomedical waste management among health workers. It focuses on health facility related factors affecting poor BMWM, individual related factors affecting poor BMWM and effects of poor BMWM among health workers in Katabi hospital- Entebbe district in the area of study.

Health facility related factors contributing to poor biomedical waste management among health workers in Katabi military hospital-Entebbe district.

The study carried out in low level health facility in Dar es Salaam by comparing Ilala and Kinondoni municipalities in Tanzania revealed that; most of the facilities have no specific disposal sites. In Ilala, 70% of the health facilities burn wastes in poorly designed incinerators, open pit burning or on the ground while in Kinondoni, 83% of the facilities bury wastes in the pits. More than 50% of the disposal sites surveyed are not fenced and were in close proximity to human settlements. About 60 and 70% of incinerators in the surveyed facilities in Ilala and Kinondoni municipalities, respectively, are not in good working conditions, 50% of them being of low capacity with some parts missing, e.g., chimneys, ash pits, covers for waste loading and ash removing doors. Also, 9 and 47% of the healthcare facilities in Ilala and Kinondoni, respectively, do not have the Standard Operating Procedures. Medical waste transportation is a serious problem, as 71% of the facilities in Kinondoni carry the wastes on hands to the disposal sites while in Ilala, 40% of LLHFs use wheelbarrows. Waste segregation and color coding are poorly adhered to while most of the storage areas are too small. It was concluded that, the medical waste management in LLHFs is still poor. Awareness should be raised among LLHFs workers on proper management of the medical waste (SV Manyele, 2010).

A qualitative cross section study conducted in 30 of 52 health facilities in kumbo east and kumbo west health districts reveled that in 86.7% of health facilities, waste disposal was by burning in pits located within 400m away from the facility.

These pits were not protected from scavengers. Only 4 facilities had incinerators and all did not meet the required standards, as none was equipped with a scrubber. Even after segregation at the point generation, wastes were mixed at the point of final disposal. Waste bins were not color-coded and all facilities had appropriate safety boxes for sharps. (Gillian Dzekashu, 2017)

A study carried out on poor medical waste management practices and its risks to human health and environment showed that open dump sites in facilities are not even engineered or treated, thus exposed the entire public to risks of infection. All the hospitals sampled do not have any unit or department responsible for waste management. Also waste management with safe and environmentally sound methods cannot be over-emphasized thus Solid waste disposal methods indicated that open dump sites were most preferred while incineration was nonexistent in the hospitals, clinics. Most other hospitals do not segregate wastes into marked or color coded containers for the different waste streams neither do they keep records of waste generation and disposal (Garba, 2013)

A cross section study carried out on factors influencing adherence to proper health care waste management practices among health workers in Wakiso district, Uganda showed that most health facilities have 10 to 25 health care waste handlers (85.6 %%) while a very negligible proportion (0.75%) of them have more than 45 HCW handlers. It also revealed that the type and size of the health facility affects the compliance to

HCWM of solid wastes and self-contained onsite treatment methods are more desirable and feasible in large public healthcare facilities but are impractical or uneconomical for smaller health facilities; and logically the size of the health facility dictates the mode of waste management (Josephine Babirye, 2020)

2.2 Individual related factors contributing to poor biomedical waste management among health workers in Katabi military hospital- Entebbe district

The main factors in this group include knowledge, attitudes and practices about poor biomedical waste management among health workers.

A quantitative study carried out in jawah-lah showed that knowledge regarding the hazardous nature of BMW is much lower than expected standards especially among nursing staff and class 4 workers (12.5%) and 13.33% respectively, whereas awareness among doctors was lower than expectations (53.33%). The knowledge regarding the correct duration of storage of BMWS was poor amongst both nursing staff 31.75% and class 4 (66%), however their knowledge about BMW as a disease source was greater in nursing staff (93.75%); 80% in class 4. Disappointingly only 42.83% of doctors and 31.25% of nursing staff had received BMW management training (Mohit, 2017).

Biomedical waste management is still at the infancy stage and recently got attention due to increased awareness about human immunodeficiency virus, hepatitis B virus, hepatitis C virus, and other potentially infectious diseases. Biomedical waste can transmit more than 30 dangerous blood borne pathogens. A systemic review of 150 articles published since 2,000 revealed that at least 50% of the world population is threatened by public health risks due to mismanagement of BMWs. This is because any carelessness of BMWM can spread infections and contaminate the entire environment (Teshiwal, 2018).

Segregation has been identified as an important aspect of healthcare waste management. It refers to the process of separating healthcare waste into various selected or labeled categories. This is significant towards ensuring the safe management of healthcare waste as it entails that all waste should be separated from general waste at the source of generation (Sambo, 2017).

Injections with contaminated needles and syringes in low and middle-income countries have reduced substantially in recent years, partly due to efforts to reduce reuse of injection devices.

Despite this progress, in 2010, unsafe injections were still responsible for as many as 33,800 new HIV infections, 1.7million hepatitis B infections and 315,000 hepatitis C infections (WHO,2018).

Attitude among participants of the study regarding BMW management was encouraging especially in terms of realizing their responsibility towards waste management and volunteering to be a part of waste management team (greater than 90% in all 3 groups) (Kapoor, 2015).

One–fourth participants (26.14%) showed unfavorable attitude towards biomedical waste management. Most of participants 159(90.34%) felt poor handling of biomedical waste is an important issue and a matter for concern and it's a part of their duty but 69(39.2%) felt that it was an extra burden on work (Vanesh, 2016).

2.3 Effects of poor BMWM among health workers in Katabi military hospital– Entebbe district

A person who experiences one needle stick injury from a needle used on an infected source patient has risk of 30%, 1.8%, and 0.3% respectively of becoming infected with Hepatitis B virus (HBV), Hepatitis C virus (HCV) and HIV (WHO, 2018).

A total of 80% of the waste generated in the hospitals is composed of general waste while the remaining 20% comprises of infectious, toxic or radioactive waste. Of this, 20% of the waste is highly infectious and dangerous and could cause serious damage to the society and the environment when it is not properly segregated and disposed of (Joseph, 2015).

Diseases associated with poor medical waste management include nosocomial diseases, typhoid, skin disorder, intestinal parasitosis and hepatitis. In addition, there is a potential risk of

HIV transmission to a susceptible human host from percutaneous injury by infected sharps (Julius, march 2015).

Poor medical waste management causes environmental pollution, unpleasant smell, growth and multiplication of insects, rodents and worms, and may lead to transmission of diseases like typhoid, cholera, and hepatitis through injuries from sharps contaminated with blood (Garba, 2013)

Medical waste is also a source of contamination of land and water sources if not rendered harmless before its burial on land or disposal in water. Furthermore, medical waste emits harmful gases, which leads to atmospheric pollution, when treated in open burning or burning in incinerators. These emissions can cause respiratory and skin diseases or even cancer, if precautionary protocols are ignored (Ibrahim, 2013).

III. CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter describes the area of study, study design, study population, sampling procedure, sample size determination, tools for data collection, data analysis and presentation, ethical consideration and dissemination of results.

3.2 Study Area

The study was conducted in Katabi Military Hospital. The health facility is a district hospital that has several wards and serves a population of approximately 0.5million people from the Katabi municipal council, Entebbe town.

Katabi military hospital is located on the Entebbe road, in the town of Katabi town counsel, in Entebbe district.

District, about 0.5 kilometres west Entebbe Region Hospital. This is approximately 40 kilometres (25mi), south of Mulago National Referral Hospital. The coordinates of Katabi Military hospital are: 0005'01.0" N, 32028'50.0" E (Latitude:0.083612; Longitude:32.480557)

3.3 Study Design

A descriptive cross section study was carried out to access the factors contributing to poor management of bio-medical waste among health workers in Katabi health center using both qualitative and quantitative data.

3.4 Study Population

The study included health workers in Katabi health center IV to assess the factors contributing to poor management of bio-medical waste among health workers in Katabi health center.

3.5 Sample Size Determination

The sample size was determined using the Kish and Leslie formula (1965);

$$N = \frac{Z^2PQ}{d}$$

Where;
N = desired sample size
P = Estimated population of desired characteristics
Z = standard deviation taken as 1.65 at a confidence level of 95%
If there is no measured estimate, we use 50% (constant) or 0.5 therefore:
P = 75%=0.75
d=Degree of accuracy desired 0.1 or 10% and in this case 95% confidence level has 10% errors, therefore 0.1 is a significance level.
q=Represents (1-p) where, q=0.25

$$N = \frac{(1.65)^2 \times 0.75 \times 0.25}{(0.1)^2}$$

N=51.046875
N=51 respondents

Therefore, the researcher will consider 50 respondents from Katabi Health center IV who were available for the study.

3.6 Sampling technique

Convenience sampling method was used where health workers easy to contact or reach will be involved in the study.

3.7 Sampling Procedure

Convenience sampling method was used where health workers available and easy to reach will be involved in the study.

This method involved the sample being drawn from the part of the population that was close to hand. People who are willing and available to participate were used in the study. The method was cheap, easy to conduct and the data needed is readily available.

3.8 Data Collection Procedure

The researcher got approval of the study from Kampala School of Health Sciences and thereafter was issued with an introductory letter to the Medical Superintendent Katabi hospital. The researcher introduced herself to the health workers at Katabi hospital. A consent form was issued to the participants for data collection. Questionnaires were used to obtain data during the study.

3.9 Data Collection Tools

The data was collected using semi-structured questionnaires of 21 open and closed ended questions.

3.9.1 Questionnaire

This tool was used because large amounts of information was collected from a large number of people in a short period of time and was relatively cost effective.

3.10 Quality Control

The forms were checked for completeness before the respondent level to ensure that the methodology was able to answer the objectives of the study.

The questionnaire was pre-tested and administered to 10 respondents among health workers in Katabi hospital and adjustments were made appropriately basing on their responses.

The data collection tools were designed appropriately to ensure that they are of quality for example; questionnaires are structured with non-ambiguous and well-spaced questions to avoid congestion and provide tidy work.

3.11 Inclusion and Exclusion Criteria

3.11.1 Inclusion Criteria

All health workers of Katabi military hospital present during the period of data collection.

3.11.2 Exclusion Criteria

All health workers of Katabi Military hospital absent and did not consent to the study.

3.12 Data Analysis and Interpretation

Data was collected coded and entered into Microsoft Office Excel. Descriptive (univariate) data was presented as frequencies and percentages, and illustrated using frequency tables, pie charts and bar graphs. Qualitative data collected during the interviews was coded in themes and entered into master sheets by the researcher. Data was analyzed manually using Pearson Chi-square independent content analysis technique and findings integrated during report writing in form of quotes and narratives to supplement the quantitative data.

3.13 Ethical Considerations

The proposal was approved by the research committee of the school and an introductory letter was obtained from the school that introduced the researcher to the Medical superintendent (MS) Katabi hospital. Permission to collect data was obtained from the MS Katabi hospital.

An informed written consent was sought from respondents who will be assured of confidentiality of the information provided.

To ensure anonymity, the names of the respondents were not stated on any data collection tool.

3.14 Study limitation

Some respondents refused to disclose the information needed from them and this was reduced by guaranteeing maximum confidentiality and privacy.

The researcher was faced with financial problems due to lack of money for necessities like transport and research was tiresome. The researcher had to move from school to the health center and other various areas to collect and process data.

Some respondents were not able to understand the language used and therefore there was a need to hire interpreters.

3.15 Anticipated limitations and possible solutions of the study

The researcher faced financial difficulties. However, the researcher solicited for the required resources to complete the study within the required time frame and a budget to direct the required expenditure was developed and followed effectively.

Some respondents were not willing to participate in the study and this was solved by fully explaining purpose of the study to them and informed consent was obtained from the respondents before participating in the study.

Some respondents were not willing to reveal some important information as it could be treated as confidential to them. This was solved by explaining the purpose of the study to the respondents and assuring them with confidentiality of their information.

3.16 Dissemination of information

The findings were compiled and printed, three copies were produced and submitted to UAHEB, KSHS, Katabi Health Centre IV, supervisor and finally to the researcher.

IV. CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter consists of data analysis, presentation and interpretation and therefore it encompasses a summary of the findings from the data collected. Data for this study was collected by use of questionnaires guided by use of operational definition of variables in chapter three to meet the objectives of the study.

Respondents to these questionnaires were health workers in Katabi hospital. Health workers were interviewed by simple random sampling technique and the finding were then tabulated for presentation in summarized format guided by the objectives of the study as below.

4.2 Demographic data

Table 1: Shows the distribution of respondents according to their demographic features

Variables	Frequency (f)	Percentage (%)
Age		
20-29	18	36
30-39	25	50
40-49	2	4
50 and above	5	10
Total	50	100

Sex		
Female	17	34
Males	33	66
Total	50	100
Marital status		
Married	12	24
Single	20	40
Widowed	11	22
Divorced/separated	7	14
Total	50	100
Profession		
Nurse	21	42
Clinical officer/doctor	10	20
Midwife	15	30
Pharmacist/Pharmacy technician	4	8
Total	50	100

From the table above, most (50%) of the respondents were aged between 30-39 whereas least (4%) of the respondents were aged between 40-49.

Furthermore, basing on sex, most (66%) of the respondents were males whereas least (34%) of the.

Furthermore, basing on marital status, most (40%) of the respondents were single whereas least (14%) of the respondents were divorced/ separated.

In conclusion, basing on profession, most (42%) of the respondents were nurses whereas least (8%) of the respondents were pharmacists/ pharmacy technicians.

4.3 Facility related factors contributing to poor biomedical waste management

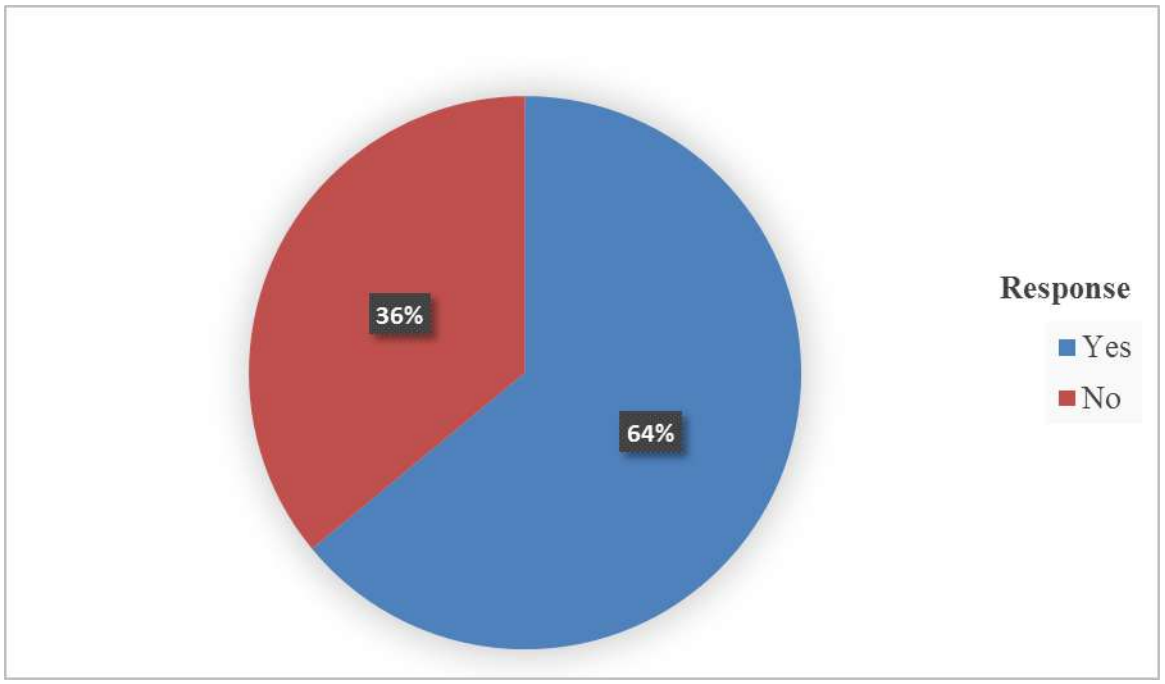

Figure 1: Shows the distribution of respondents according to if their different types of wastes generated

From the figure above, most (64%) of the health workers agreed that there were different types of wastes generated whereas the least (36%) of the health workers disagreed.

Table 2: Shows the distribution of respondents according to the different types of wastes generated in the hospital

Waste generated	Frequency	Percentage
Cotton	12	37.5
Needle	8	25
Syringes	3	9.3
Gauze	4	12.5
Cannulas	2	6.25
Ampoules	3	9.3
Total	32	100

From the table above, most (37.5%) of the respondents said that cotton wastes were generated whereas least (6.25%) said that ampoule wastes were generated.

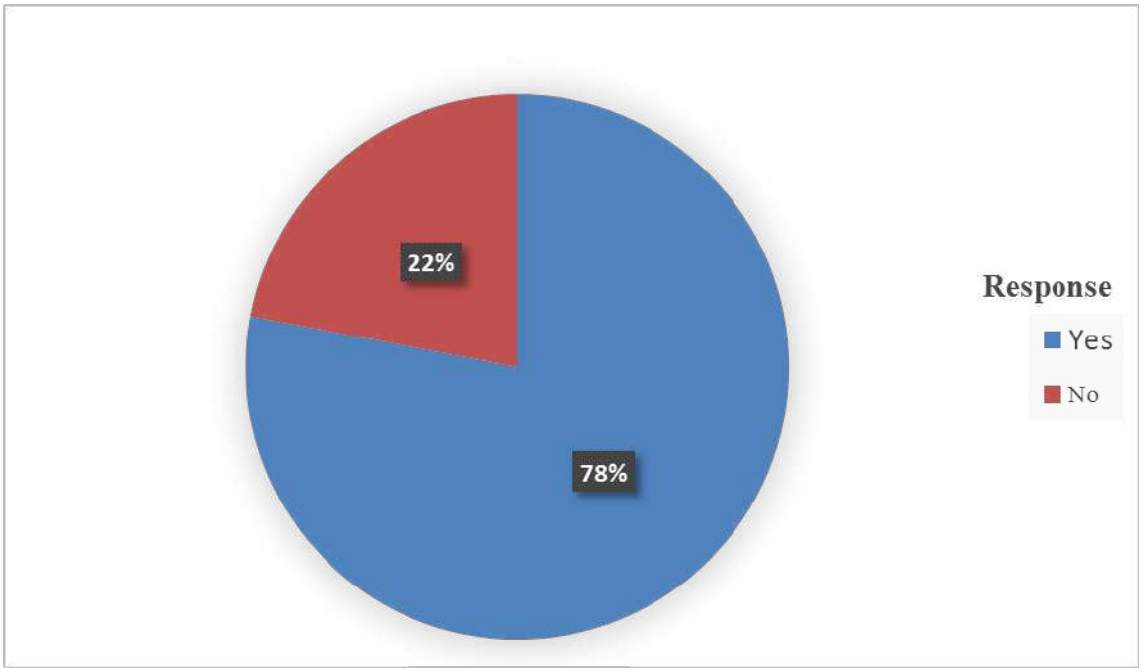

Figure 2: Shows the distribution of respondents according to biomedical waste management plan

From the figure above, majority (78%) of the respondents agreed that the hospital has a biomedical waste management plan whereas minority (22%) disagreed

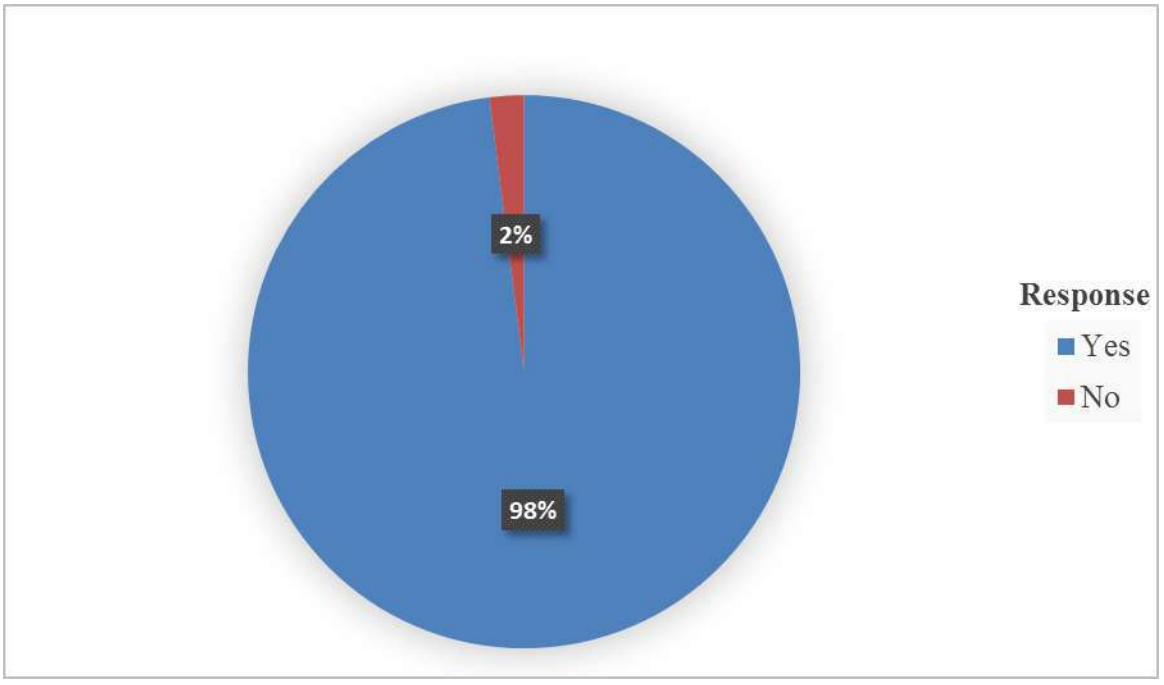

Figure 3: Shows the distribution of respondents according to whether the hospital has color- coded bins

From the figure above, majority (98%) of the respondents agreed that the hospital has color coded bins whereas minority (2%) disagreed.

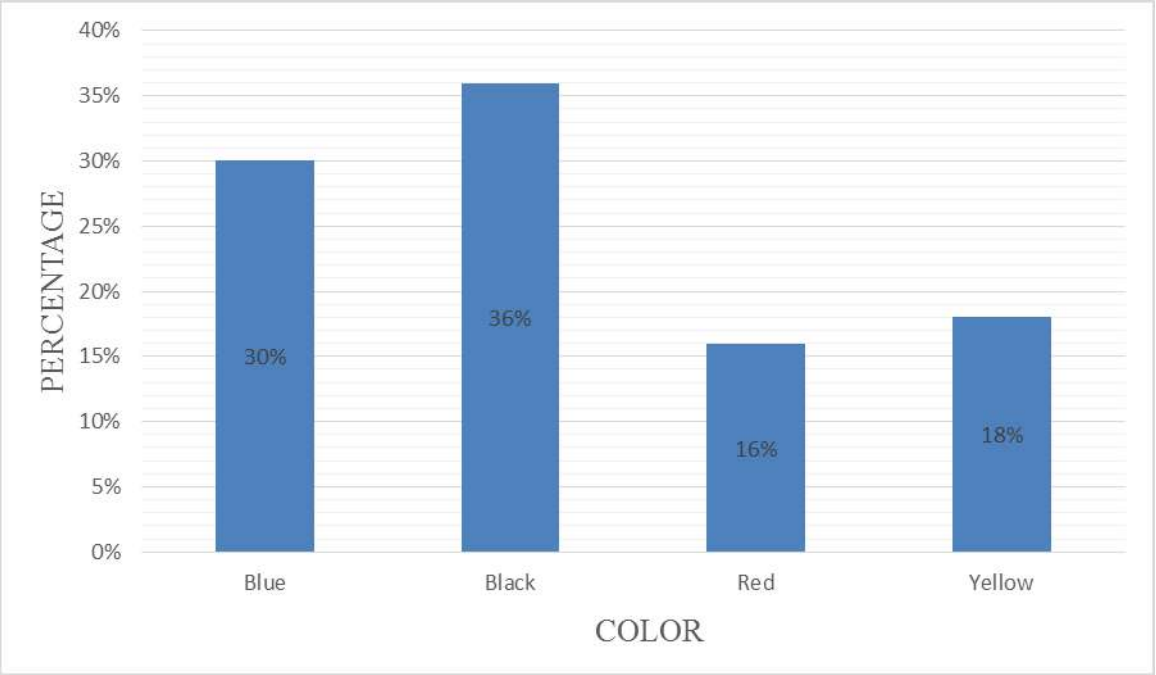

Figure 4: Shows the distribution of respondents according to the color of coded bins were coded black whereas least (16%) of the respondents said that the bins were coded red

From the figure above, most (36%) of the respondents said that the bins were coded black whereas least (16%) of the respondents said that the bins were coded red.

Table 3: Shows the distribution of respondents according to method of disposal used

Response	Frequency	Percentage
Incineration pits	24	48
Landfills	10	20
Pits	11	22
Others	5	10
Total	50	100

From the table above, most (48%) of the respondents said that incinerator pits were the method of disposal used whereas least (5%) of the respondents said that other methods of disposal were used.

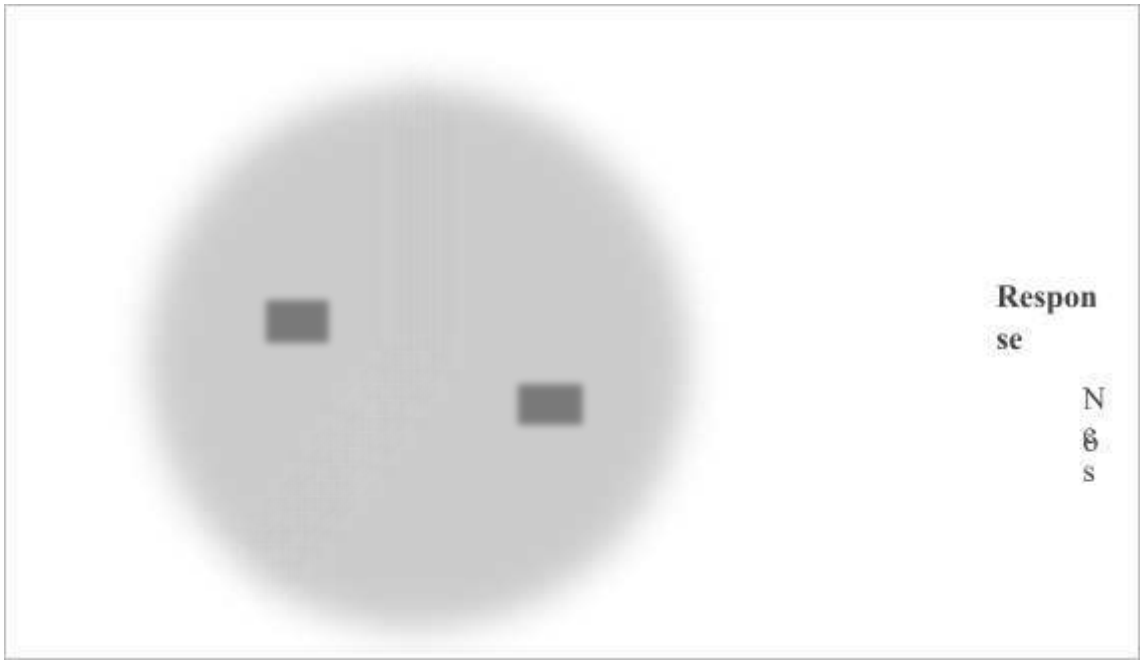

Figure 5: Shows the distribution of respondents according to if the size of the hospital contributes to poor biomedical waste management

From the table above, most (60%) of the respondents agreed that the size of the hospital contributes to poor biomedical waste management whereas least (40%) agreed otherwise.

4.4 Individual related factors contributing to poor biomedical waste management among health workers

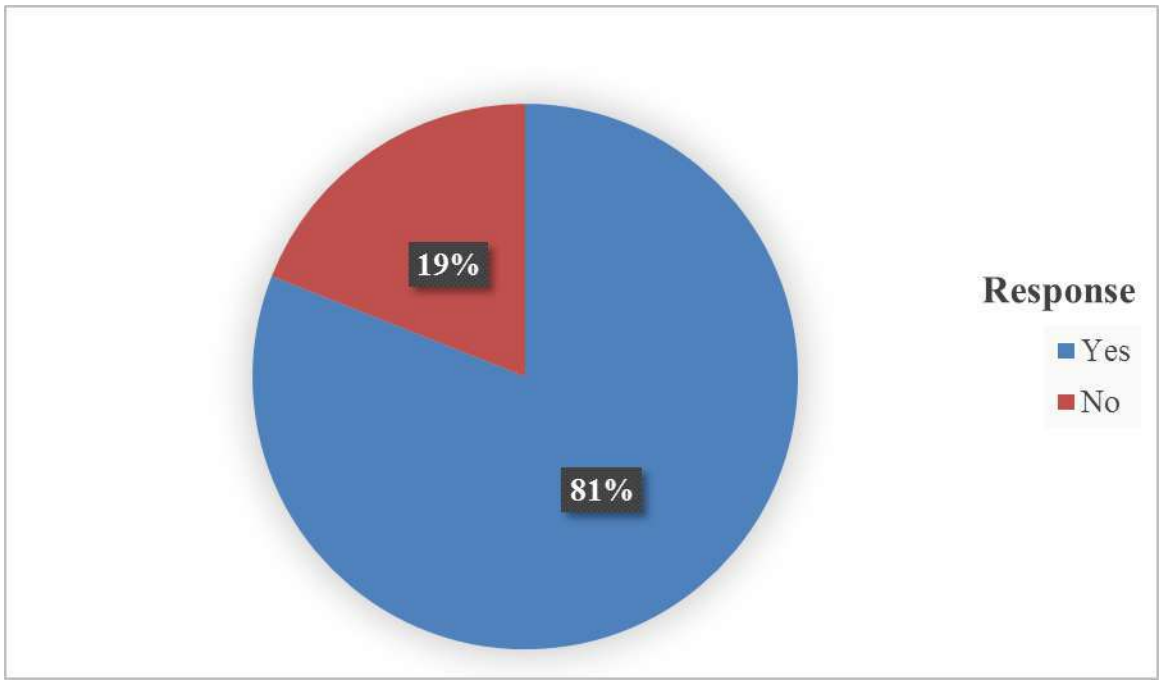

Figure 6: Shows the distribution of respondents according to information about biomedical waste management

From the figure above, majority (81%) of the respondents agreed that they have heard about information regarding biomedical waste management whereas minority (19%) of the respondents agreed otherwise.

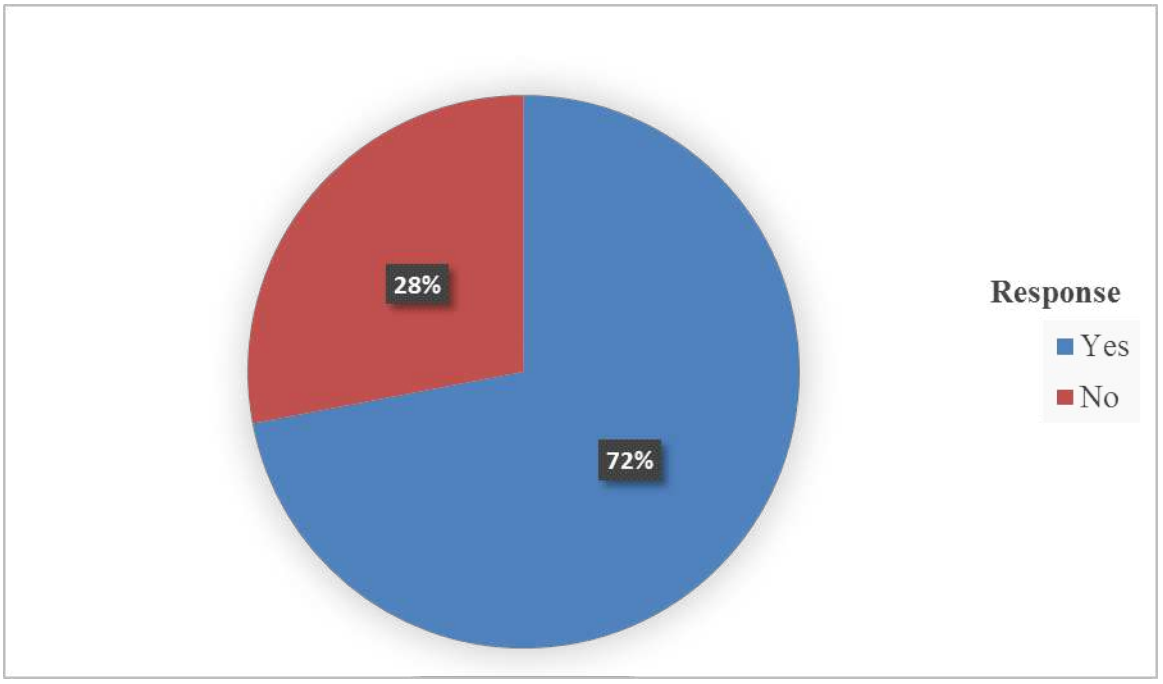

Figure 7: Shows the distribution of respondents according if they segregate biomedical wastes depending on different categories

From the figure above, majority (72%) of the respondents agreed that they segregate biomedical wastes depending on different categories whereas minority (28%) of the respondents agreed otherwise.

Table 4: Shows the distribution of respondents according to which color-coded bin they dispose syringes, needles, cotton and contaminated gauze

Bin color	Frequency(f)	Percentage (%)
Red bin	12	33.3
Blue bin	9	25
Black bin	5	13.8
General Bin	10	27
Total	36	100

From the table above, most (33.3%) of the respondents said that they dispose syringes, needles, cotton and contaminated gauze in a general bin whereas least (13.8%) of the respondents said that they dispose syringes, needles, cotton and contaminated gauze in a red bin.

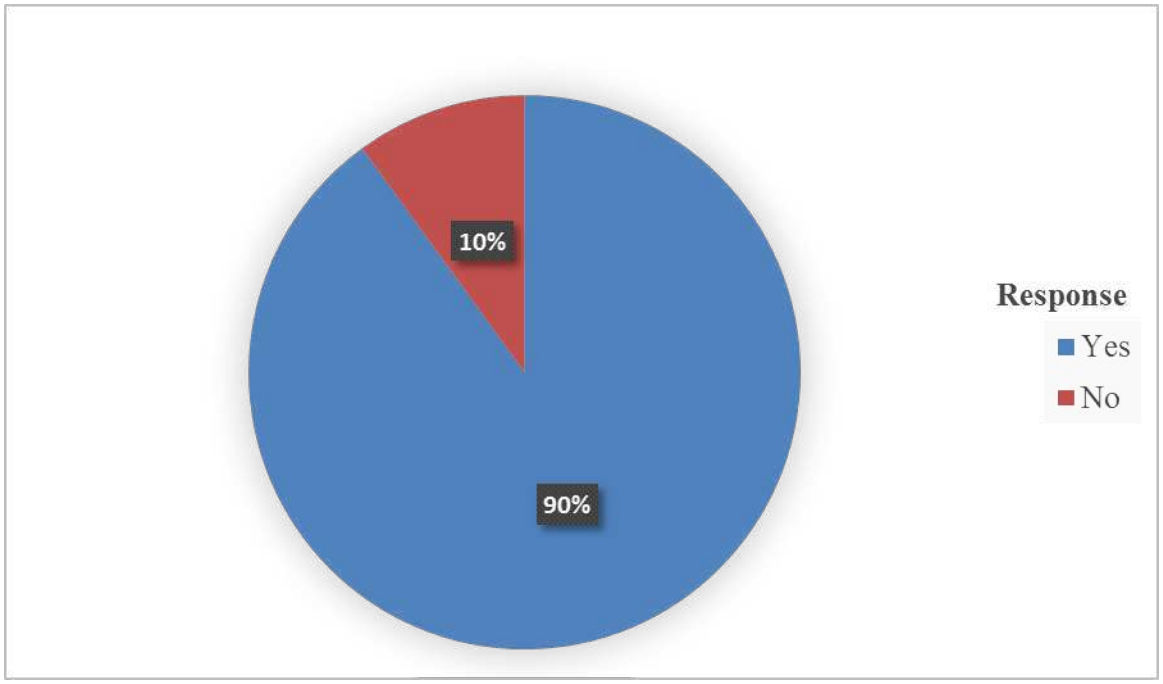

Figure 8: Shows the distribution of respondents according to the use of personal protective equipment when disposing biomedical wastes

From the figure above, majority (90%) of the respondents agreed that they use personal protective equipment's when disposing biomedical wastes whereas minority (10%) agreed otherwise.

Table 5: Shows the distribution of respondents according to which personal protective equipment they use in the hospital

Personal protective equipment	Frequency(f)	Percentage (%)
Gloves	18	40
Apron	7	15.5
Masks	8	17.8
Boots	10	22.2
Others	2	4.4
Total	45	100

From the table above, most (40%) of the respondents said that they use gloves whereas least (4.4%) of the respondents said that they use aprons.

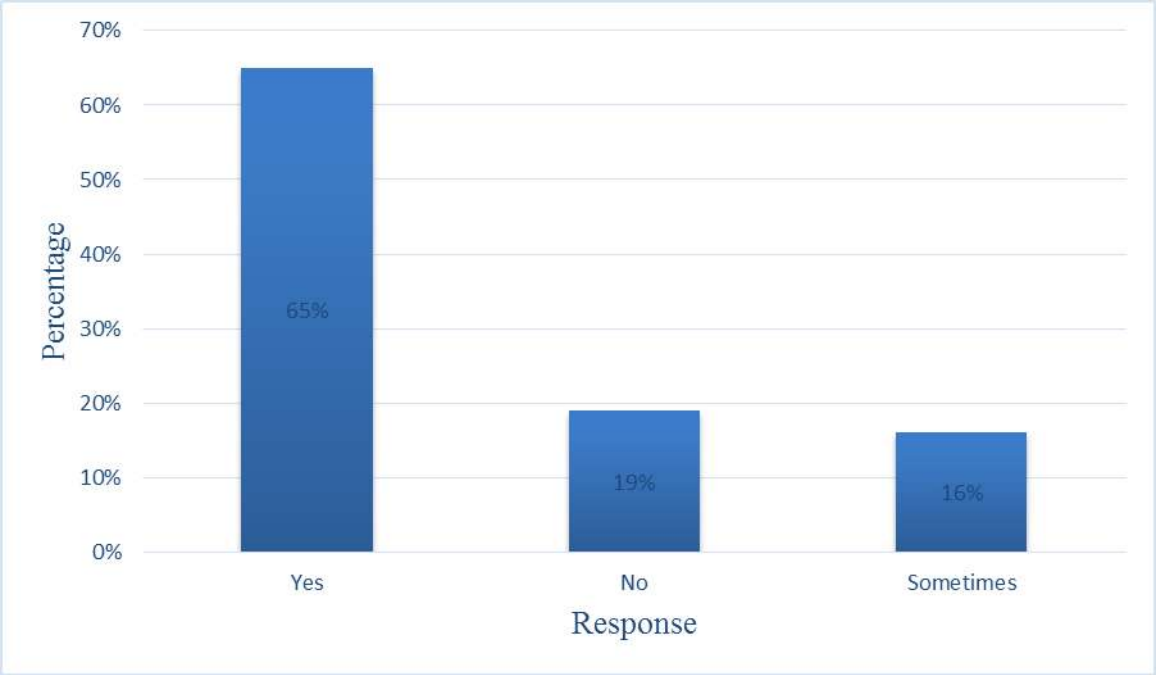

Figure 9: Shows the distribution of respondents according to whether biomedical waste management is an extra burden to work

From the table above, most (65%) of the respondents said that biomedical waste management is an extra burden to work whereas least (16%) of the respondents said that sometimes biomedical waste management is an extra burden to work.

4.5 Effects of poor biomedical waste management among health workers

Table 6: Shows the distribution of respondents depending on whether poor biomedical waste management can cause environmental pollution, unpleasant smell and multiplication of insects, rodents and worms

Response	Frequency(f)	Percentage (%)
Yes	40	80
No	3	6
I don't know	1	2
Sometimes	6	12
Total	50	100

From the table above, majority(80%) of the respondents said that poor biomedical waste management can cause environmental pollution, unpleasant smell and multiplication of insects, rodents and worms whereas minority (2%) of the respondents said that they didn't know if poor biomedical waste management can cause environmental pollution, unpleasant smell and multiplication of insects, rodents and worms.

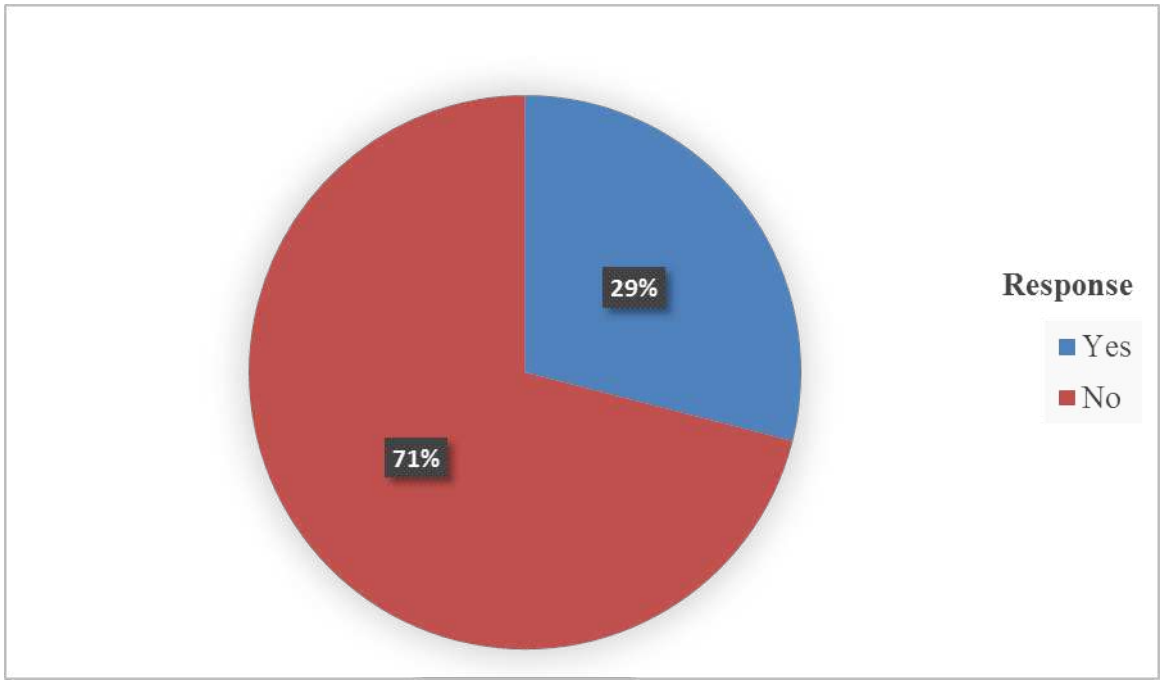

Figure 10: Shows the distribution of respondents according to if poor biomedical waste management causes accidents like needle stick injury

From the figure above, majority (71%) of the respondents agreed that poor biomedical waste management causes accidents like needle stick injury whereas minority (29%) of the respondents agreed otherwise.

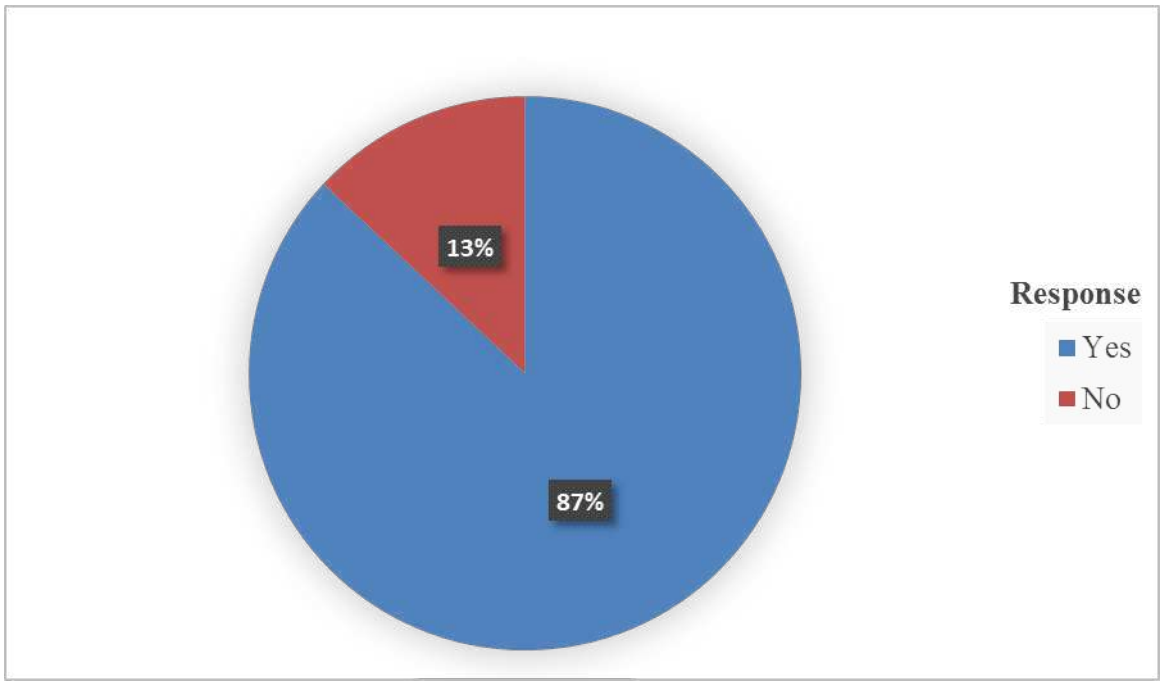

Figure 11: Shows the distribution of respondents according to if poor biomedical waste management can cause illnesses

From the figure above, majority (87%) of the respondents agreed that poor biomedical waste management can cause illnesses whereas minority (13%) of the respondents disagreed.

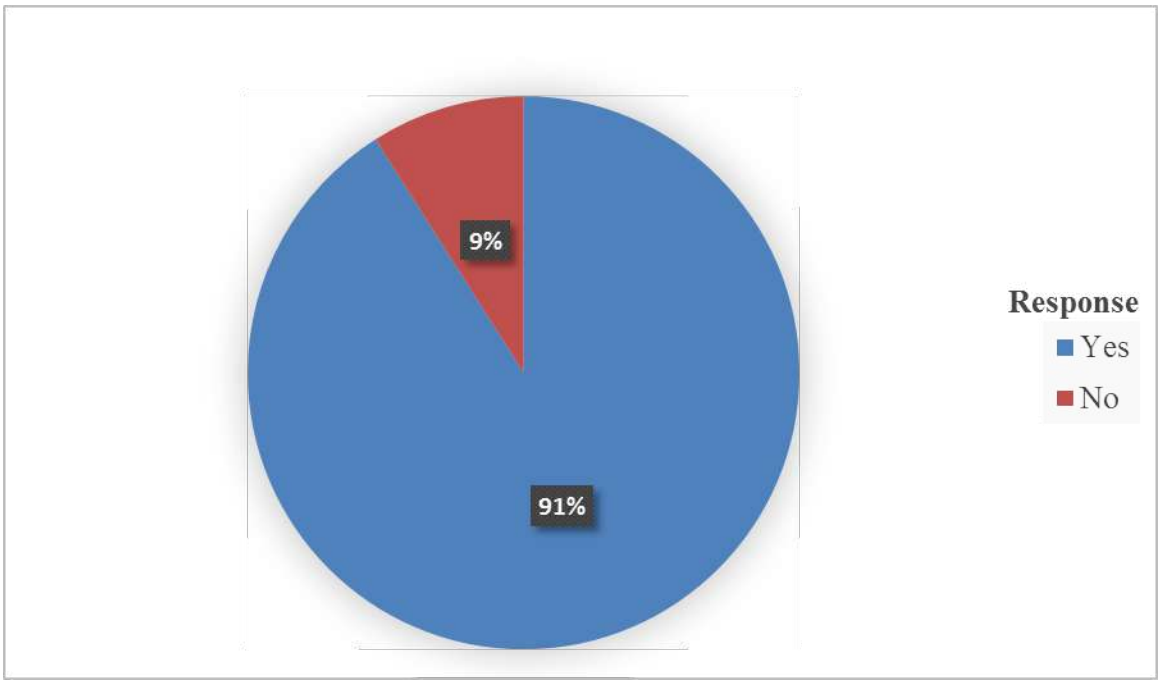

Figure 12: Shows the distribution of respondents according to if poor bio medical waste management can cause nosocomial diseases and skin disorders

From the figure above, majority (91%) of the respondents agreed that poor biomedical waste management can cause nosocomial diseases and skin disorders whereas minority (9%) of the respondents agreed otherwise.

V. CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMEDATIONS

5.1 Introduction

This chapter contains discussion of results, conclusions and recommendations. The study discussed the factors contributing to poor biomedical waste management among health worker. The findings were discussed under the following themes; Healthy facility-related factors, individual related factors contributing to poor biomedical waste management among health workers such as knowledge, attitude and practice and effects of poor biomedical waste management among health workers.

5.2 Discussion of results

Health-facility related factors contributing to poor biomedical waste management among health workers.

Most (48%) of the respondents said that the hospital has no well-designed incinerator pit sites for waste disposal hence making segregation and waste management difficult since pits were not protected from scavengers thus contributing to poor biomedical waste management among health workers and this finding is in line with the a qualitative cross section study conducted in 30 of 52 health facilities in kumbo east and kumbo west health districts reveled that in 86.7% of health facilities, waste disposal was by burning in pits located within 400m away from the facility. These incinerator pits were not protected from scavengers. Only 4 facilities had incinerators pits and all did not meet the required standards, as none was equipped with a scrubber. Even after segregation at the point generation, wastes were mixed at the point of final disposal. Waste bins were not color- coded and all facilities had appropriate safety boxes for sharps. (Gillian Dzekashu, 2017).

Majority of the respondents (60%) agreed that size of the hospital contributes to poor biomedical waste management due to large quantity of wastes

generated yet disposal methods such as incineration, pit burning and burying are not practically done well thus compliance and adherence to proper waste management becomes a challenge and this study finding correlate with a cross section study carried out on factors influencing adherence to proper health care waste management practices among health workers in Wakiso district, Uganda showed that most health facilities have 10 to 25 health care waste handlers (85.6 %%) while a very negligible proportion (0.75%) of them have more than 45 HCW handlers. It also revealed that the type and size of the health facility more desirable and feasible in large public healthcare facilities but are impractical or uneconomical for smaller health facilities; and logically the size of the health facility dictates the mode of waste management (Josephine Babirye, 2020).

Individual related factors contributing to poor biomedical waste management among health workers

Majority of the respondents (81%) had ever received any information about biomedical waste management such as methods of waste disposal, segregation of wastes and waste treatment before disposal. This finding does not correlates with a quantitative study carried out in jawah-lah which showed that knowledge regarding the hazardous nature of BMW is much lower than expected standards especially among nursing staff and class 4 workers (12.5%) and 13.33% respectively, whereas awareness among doctors was lower than expectations (53.33%). The knowledge regarding the correct duration of storage of BMWS was poor amongst both nursing staff 31.75% and class 4 (66%), however their knowledge about BMW as a disease source was greater in nursing staff (93.75%); 80% in class 4. Disappointingly only 42.83% of doctors and 31.25% of nursing staff had received BMW management training (Mohit, 2017).

Most of the respondents (65%) felt that biomedical waste management is an extra burden on their work since most times they are occupied by hospital work like attending to emergencies and other patients of all kinds hence no time to practice proper biomedical waste disposal hence poor biomedical waste management and this finding is in line with the study which indicated that One – fourth participants (26.14%) showed unfavorable attitude towards biomedical waste management. Most of participants 159(90.34%) felt poor handling of biomedical waste is an important issue and a matter for concern and it's a part of their duty but 69(39.2%) felt that it was an extra burden on work (Vanesh, 2016).

Majority (72%) of the respondents segregate biomedical wastes according to different categories especially at the time of segregation hence protection from the injuries though sometimes they don't segregate at the time of generation due to work overload and pressure generated by the patients during treatment and this finding is in line with the study which showed that segregation has been identified as an important aspect of healthcare waste management. It refers to the process of separating healthcare waste into various selected or labeled categories. This is significant towards ensuring the safe management of healthcare waste as it entails that all waste should be separated from general waste at the source of gen3e0ration (Sambo, 2017).

Effects of poor biomedical management among health workers in Katabi hospital in Entebbe district

Majority (91%) of the respondents agreed that poor biomedical waste management cause nosocomial diseases and skin infections. Other diseases include typhoid, cholera, HIV/AIDS, hepatitis which increases hospital visits and loss of lives. This finding is in line with the study which showed that diseases associated with poor medical waste management include nosocomial diseases, typhoid, skin disorders, intestinal parasites and hepatitis. In addition, there is a potential risk of HIV transmission to a susceptible human host from percutaneous injury by infected sharps (Julius, March 2015)

Majority of the respondents (80%) agreed that poor biomedical waste management cause environmental pollution, unpleasant smell and multiplication of insects, rodents and worms which leads to spread of infections which can be

life threatening and this study is in line with the study which showed that Poor medical waste management causes environmental pollution, unpleasant smell, growth and multiplication of insects, rodents and worms, and may lead to transmission of diseases like typhoid, cholera, and hepatitis through injuries from sharps contaminated with blood (Garba, 2013).Also it is in line with the study which showed that Medical waste is also a source of contamination of land and water sources if not rendered harmless before its burial on land or disposal in water.

Furthermore, medical waste emits harmful gases, which leads to atmospheric and environmental pollution, when treated in open burning or burning in incinerators. These emissions can cause respiratory and skin diseases or even cancer, if precautionary protocols are ignored (Ibrahim, 2013).

Majority of the respondents (71%) agreed that poor biomedical waste management causes accidents like needle stick injury especially from those which are already used and they are infectious hence many people ending up getting infected with hepatitis, HIV and this in line with the study which showed that a person who experiences one needle stick injury from a needle used on an infected source patient has risk of 30%, 1.8%, and 0.3% respectively of becoming infected with Hepatitis B virus (HBV), Hepatitis C virus (HCV) and HIV (WHO, 2018).And also it in the same line with the study which showed that a total of 80% of the waste generated in the hospitals is composed of general waste while the remaining 20% comprises of infectious, toxic or radioactive waste. Of this, 20% of the waste is highly infectious and dangerous and could cause serious damage to the society and the environment when it is not properly segregated and disposed of (Joseph, 2015).

VI. CONCLUSIONS

Social-demographic characteristics of the study participants were: majority of the respondents were aged between 30-39 years (50%), males were more than females (66%), single (40%), Majority of respondents were nurses (42%).

Concerning individual related factors about BMWM, (81%) had some knowledge about biomedical waste management and majority (72%) of the respondents were segregating wastes according to their different categories as required in different color coded bins and most were using personal protective equipment while disposing off the wastes.

Practices of health workers about BMWM were; disposing all kinds of waste into general bin.

Not segregating the biomedical waste according to different categories, denying that they had training on biomedical waste handling and disposal.

Effects of poor BMWM were; poor disposal of medical wastes contaminates water sources, poor disposal of pharmaceutical wastes leads to diseases like cancer, causes accidents, waste is highly infectious and dangerous and cause serious damage to the society and the environment, lead to transmission of diseases like typhoid, cholera, and hepatitis through injuries from sharps contaminated with blood, hazardous and toxic parts of waste from healthcare establishments comprising infectious, medical and radioactive material as well as sharps constitute a grave risk to mankind and the environment.

VII. RECOMMENDATIONS

Recommendations to Policy makers and Government agents

Following the conclusions above, the following recommendations should be considered:

1. The Government and other stake holders should ensure that the health workers receive trainings on how to manage wastes of any form and supplies to be used should be readily available and should be taught on how to use them.
2. The district health service provider should intensify effective health education of the community, paying special attention to waste disposal management education and communication materials geared towards sensitizing them so as to reduce the incidence of pollutions and raising infections.

3. The DHO should work with and facilitate administrators, village health teams to promote good sanitary environment to reduce on the incidences of injuries from dumped sharp materials and infectious materials to both the staff and community at large.

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I acknowledge my mother Mrs. Nalubwama Evelyn, my friend Lakop Esther Faith who have tirelessly stood with me in all times of struggle both academically and socially, my supervisor Mr. Nimwesiga Gordon who has always been there for me as my role model where he has always guided me about my career and for all their support towards my academic struggles.
May God bless them all.

List of Abbreviations and Acronyms

BMWM:	Biomedical Waste Management
BMWs:	Biomedical Wastes
HCFs:	Health-Care Facilities
HCWM:	Health-Care Waste Management
HCWs:	Health-Care Wastes
MS:	Medical Superintendent
MW:	Medical Waste
MWHs:	Medical Waste Handler
MWM:	Medical Waste Management
UAHEB:	Uganda Allied Health Examination's Board
WHO:	World Health Organization
KMH:	Katabi Military Hospital
DHO:	District Health Officer

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Appendices Appendix I: Consent Form

Dear respondents, my name is Masagazi Edward, a pharmacy student at Kampala School of Health Sciences pursuing a diploma in pharmacy; doing a study on "Factors contributing to poor biomedical waste management among health workers in Katabi Military hospital in Entebbe District." The study is basically for my academic purpose; I humbly request for your complete participation and the information given shall remain confidential. For your participation, the process of the study has no payment, or special benefit. I can assure that the study also has no any physical or psychological trauma as well as political problem, but participation in the study by giving correct answers can play great role in the successfulness of the study and also it will provide great input to bring change in quality of health. Therefore, you are kindly requested to respond genuinely and voluntary with patience. To fill these questions, it may take 25 minutes.

Respondent's Consent

I consent to participate in this study and I am aware that the study is purely academic, my participation is voluntary, and my responses are to the best of my knowledge and belief and will be treated with the utmost confidentiality.

Respondent's signature..... Date: .....

Appendix II: Questionaire

Dear respondents, my name is Masagazi Edward, a pharmacy student at Kampala School of Health Sciences pursuing a diploma in pharmacy; doing a study on "Factors contributing to poor biomedical waste management among health workers in Katabi hospital in Entebbe District. "The purpose of this study is purely academic. Kindly do request for your assistance by sparing some of your precious time to participate in this study. The study will take about limited time 20-30 minutes only. All information provided will be handled and treated with utmost confidentiality.

Instructions

Do not mention your name and feel free to mention what you know about the question.

A tick (√) will be used in a box provided or answer sheet written by interviewer in the space provided against each question.

SECTION A

Demographic data

1. Age of the respondent
   (a) 20-29 (b) 40-49 (c) 30-39 (d) 50 and above
2. Sex of the respondent
   (a) Female (b) Male
3. What is your marital status?
   (a) Married (b) Widowed (c) Single (d) Divorced/ separated
4. What is your profession?
   (a) Nurse (b) Midwife (c) Clinical officer/doctors (d) Others (specify)

SECTION B: Facility related factors contributing to poor biomedical waste management among health workers in Katabi military Hospital-Entebbe district

5. Are there different types of wastes generated by Katabi hospital?
   (a) Yes (b) No
6. If yes, what are these wastes?
   .....
   .....
7. Does the hospital have a biomedical waste management plan?
   (a) Yes (b) No
8. Does the hospital have color-coded bins?
   (a) Yes (b) No
9. If yes, which color-coded bins?
   (a) Blue (b) Red (c) Black (d) Yellow
10. Which disposal methods does the hospital use?
    (a) Incineration pits (b) Pits (c) Landfills (d) Others
11. Does the size of the hospital contribute to poor biomedical waste management?
    (a) Yes (b) No

SECTION C: Individual related factors contributing to poor biomedical waste management among health workers in Katabi military Hospital-Entebbe district.

12. Have you ever received any information about biomedical waste management?
    (a) Yes (b) No
13. Do you segregate biomedical wastes according to different categories?
    (a) Yes (b) No
14. Where do you dispose needles and syringes, cotton, gauze contaminated with blood?
    (a) Red bin (b) Blue bin (c) Black bin (d) General bin
15. Do you use personal protective equipment when disposing biomedical wastes?
    (a) Yes (b) No
16. Which personal protective equipment do you use?
    (a) Gloves (b) Boots (c) Apron (d) Masks (e) Others
17. Is biomedical waste management an extra burden on your work?
    (a) Yes (b) No (c) Sometimes

SECTION D: Effects of poor biomedical management among health workers in Katabi hospital in Entebbe district

18. Does poor biomedical waste management cause environmental pollution, unpleasant smell and
    (a) Yes (b) Yes (c) I don't know (d) Sometimes
19. Does poor biomedical waste management causes accidents like needle stick injury?
    (a) Yes (b) No
20. Can poor biomedical waste management cause illnesses?
    (a) Yes (b) No
21. Do you agree that poor biomedical waste management can cause nosocomial diseases and skin disorders?
    (a) Yes (b) No

Appendix III: Introduction Letter

KAMPALA SCHOOL OF HEALTH SCIENCES

P.O.BOX 14263
KAMPALA
KATALE- SEGUKU
TEL: 0700563464,
0773748592/ 0701748592,
0782413473/0704895614
Email: info@kshs.ac.ug
www.kshs.ac.ug

03/12/2021

Dear Sir/Madam,

RE: DATA COLLECTION FROM YOUR ORGANIZATION

This is to introduce to you **Mr. Masagazi Edward** who is a third year student at Kampala School of Health Sciences offering a diploma in Pharmacy.

He is conducting a study on **"Factors Contributing To Poor Biomedical Waste Management Among Health Workers In Katabi Hospital, Wakiso District"** as a partial fulfillment for the award of a Diploma.

The purpose of this communication is to request you offer him an opportunity to collect data from your organization.

Any assistance rendered to his study will be highly appreciated.

Yours faithfully,

MUBANGIZI PROSPER

PRINCIPAL

KAMPALA SCHOOL OF HEALTH SCIENCES SSEGUKU-KATALE
03 DEC 2021
P. O. BOX 14263, KAMPALA
PRINCIPAL

KATABI MILITARY HOSPITAL
05 JAN 2022
P. O. BOX 105, ENTEBBE

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Appendix IV: A Sketch Map of The study Area
kaTabi Military Hospital

Treatment of Diffuse Alveolar Hemorrhage Secondary to Systemic Lupus Erythematosus

Caicedo OA, Medina MA, Papasidero SB & Caracciolo JA

ABSTRACT

Systemic Lupus Erythematosus (SLE) is associated with numerous pleuropulmonary complications. Although rare, diffuse alveolar hemorrhage (DAH) represents a life-threatening cause of acute respiratory failure in patients with SLE.

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Treatment of Diffuse Alveolar Hemorrhage Secondary to Systemic Lupus Erythematosus

Tratamiento De La Hemorragia Alveolar Difusa Secundaria a Lupus Eritematoso Sistémico

Caicedo OA[α], Medina MA[σ], Papasidero SB[ρ] & Caracciolo JA[Ω]

RESUMEN

El Lupus Eritematoso Sistémico (LES) se asocia con numerosas complicaciones pleuropulmonares. Aunque es poco frecuente, la hemorragia alveolar difusa (HAD) representa una causa potencialmente mortal de insuficiencia respiratoria aguda en pacientes con LES.

ABSTRACT

Systemic Lupus Erythematosus (SLE) is associated with numerous pleuropulmonary complications. Although rare, diffuse alveolar hemorrhage (DAH) represents a life-threatening cause of acute respiratory failure in patients with SLE.

I. INTRODUCCIÓN

La hemorragia alveolar difusa (HAD) en pacientes con Lupus Eritematoso sistémico (LES) es una manifestación pleuro-pulmonar rara pero potencialmente catastrófica y con una alta mortalidad, caracterizada por la extravasación de glóbulos rojos hacia el espacio alveolar pulmonar debido a la interrupción de la interfaz alvéolo-capilar. La prevalencia en grandes cohortes de pacientes con LES como RELESSER y GLADEL es de 0,8 y 1,1%, respectivamente (1,2); y su incidencia varía entre 1.2 a 5.3% según series más pequeñas. Hasta un 23% de las HAD autoinmunes son secundarias a LES, otras causas posibles son las vasculitis asociadas a anticuerpos anti citoplasma del neutrófilo (ANCA), la enfermedad anti membrana glomerular así como otras enfermedades del tejido conectivo (3). La HAD debe distinguirse de otras situaciones tales como: infecciones, coagulopatías, embolismo pulmonar y edema agudo pulmonar cardiogénico y no cardiogénico (4,5). Clásicamente, el standard of care (SOC) del tratamiento consiste en pulsos de metilprednisolona (MPD) y ciclofosfamida (CF) (6,7) y, en casos refractarios, se puede recurrir a plasmaféresis (PF), inmunoglobulinas intravenosas (IGIV) (6,7) o en algunos casos a rituximab (RTX) (8).

La principal causa de infiltrados pulmonares en pacientes con LES son las infecciones pulmonares. Sin embargo, ante cuadros graves como este; la HAD debe ser considerada debido a su alta mortalidad la cual oscila entre 28 a 64% (10,11) pudiendo deberse a actividad de la enfermedad, infecciones o ambas (12,13) y las variables que se asocian a esta mortalidad son el requerimiento de ventilación mecánica, la infección nosocomial o de la comunidad, la trombocitopenia,LES neuropsiquiatrico (LESNP), el requerimiento de diálisis, el puntaje del SLEDAI y del APACHE II (10, 11,12,13,14,15).

El diagnóstico de HAD se basa en la presencia concomitante de: infiltrados alveolares densos en tres cuartas partes o más de los campos pulmonares en la radiografía de tórax; insuficiencia respiratoria de inicio agudo, y descenso de la hemoglobina mayor a 3g/dl (5,22).

La HAD puede ser la forma de presentación de la enfermedad en 10 a 20% de los casos (5) o aparecer en pacientes con LES establecido, frecuentemente asociado a nefritis lúpica activa, trombocitopenia, hipocomplementemia, compromiso neuropsiquiátrico, así como con altos puntajes en el SLEDAI (5,13,16). El síntoma más frecuente es la disnea y un 60% tienen hemoptisis en la presentación inicial (3,5). La radiografía de

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tórax muestra un infiltrado alvéolo-intersticial, alveolar bilateral o unilateral, y en raras ocasiones derrame pleural (4).

En la TC se puede encontrar la imagen de empedrado o "crazy paving", que resulta de un patrón reticular fino sobre un fondo de "vidrio esmerilado" o el signo de "bronquio obscuro" (17).

El LBA debe realizarse dentro de las primeras 48 horas con el objetivo de confirmar la HAD y excluir infección concomitante, y puede mostrar macrófagos cargados de hemosiderina (hemosiderófagos) mediante la reacción de Perls (4). Un LBA negativo no excluye la infección (9).

En casos dudosos puede recurrirse a la resonancia magnética (18) o a la biopsia pulmonar (BP) (4). La BP en pacientes diagnosticados de síndrome de distrés respiratorio agudo (SDRA) de causa desconocida ha demostrado HAD en pocos casos sin aumentar la mortalidad (19), y suele demostrar hemorragia alveolar "blanda", o sin capilaritis y depósitos de inmunocomplejos en la pared alveolar (5). Por lo que la BP podría realizarse en pacientes con LES e infiltrados pulmonares de causa no determinada e hipoxemia.

El perfil de autoanticuerpos, que incluye anti-ADN, anticoagulante lúpico, anticardiolipinas, anti-beta2-glicoproteínas I, anti-Sm, anti-Ro, anti-La y anti-RNP, no parece ser diferente en los pacientes con LES y HAD comparado con pacientes con LES sin HAD (20). Sin embargo, en pacientes con síndrome antifosfolípidos (SAF) concomitante la tromboembolia pulmonar (TEP), debe excluirse (21). No hay trabajos realizados sobre el uso de los anticuerpos como predictores de recurrencia de la HAD, así como de su utilidad en el monitoreo de la misma.

Entre un 36 a 57% de pacientes tienen una infección concomitante con la HAD al momento del diagnóstico (9,10,22). La infección al debut de la HAD o durante la internación se asocia a mayor mortalidad (9,22). El tratamiento de las mismas debe hacerse en forma empírica hasta recibir los resultados de los cultivos y en pacientes que recibían corticoterapia antes del "flare" se debería cubrir además pseudomona aeruginosa y streptococo pneumoniae resistente a betalactámicos (23), así como Staphylococcus aureus (24). Aspergillus y Citomegalovirus (CMV) deben considerarse (9). Es recomendable además buscar infecciones ocultas que podrían reactivarse con la inmunosupresión tales como tuberculosis, hepatitis B, y estrongiloidiasis (5).

II. TRATAMIENTO

El SOC de tratamiento de la HAD consiste en GC a altas dosis asociados a CF y, en casos refractarios, se puede recurrir a PF, IGIV (6,7) o en algunos casos a RTX.

El uso de GC no debe retrasarse ante el diagnóstico de HAD. La sospecha de infección no debe ser una contraindicación siempre y cuando se use concomitantemente antibióticos (4,13). A dosis de 1 mg/kg/día de prednisona no parecen aumentar la mortalidad en pacientes con SDRA (25), sin embargo, no está muy claro el efecto en pacientes con sepsis grave o shock séptico concomitante (26). No hay evidencia de alta calidad sobre cuál es la dosis diaria y cuánto debe durar el tratamiento con GC. Barile el al (22) en un estudio retrospectivo que incluyó 34 pacientes, mostró que un esquema de pulsos "masivo" de hasta 8 gramos de MPD se asoció a menor mortalidad que el esquema convencional de 3 gramos. Sin embargo, esta observación no parece reproducirse en otros trabajos (9,10,11,13). Por otro lado, hay un reporte del uso de un esquema "multitarget" en flare severo con HAD donde se redujo la dosis inicial de corticoides a no más de 20 mg/día de prednisona precedido de pulsos de 125 mg y 250 mg/día en 3 días, con respuesta favorable (27). Se necesitarían estudios con adecuada validez que intenten responder estas preguntas.

La CF es un inmunosupresor con acción sobre los mecanismos de la inmunidad celular y humoral, la frecuencia del uso de CF es variable en las distintas series (9,10,15,22), así como su efecto sobre la mortalidad. Von Ranke et al. en una revisión sistemática encontró que su uso precoz se asocia a menor mortalidad (28). No hay evidencia

de su uso en pacientes que estén cursando concomitantemente infección, por lo que sería prudente excluir la presencia de la misma.

El uso precoz de PF no tiene impacto sobre la mortalidad en pacientes con HAD (28), sin embargo, ante HAD refractaria a GC y al inmunosupresor podría usarse (6). Es recomendable el uso de PF en pacientes que tienen concomitantemente; microangiopatía trombótica (7), anticuerpos anti-MBG (29), o manifestaciones neurológicas tales como mielopatía, síndrome confusional agudo y neuropatía refractaria al SOC (30).

Las IGIV son productos biológicos con 90% IgG polivalente, extraídas de donantes individuales con efecto inmunomodulador, cuyo mecanismo de acción depende del bloqueo de receptores Fc de los macrófagos y células dendríticas, regulación de la apoptosis, neutralización de auto- anticuerpos y citoquinas, inhibición de la cascada de activación del complemento, disminución de la respuesta al INFα, y expansión de las células Treg (31). En general el uso de IGIV es seguro, aunque deben usarse con precaución en pacientes con síndrome anti fosfolípidos (SAF) concomitante ya su administración se asocia a mayor incidencia de eventos tromboembólicos (32). Se ha descrito falla renal aguda con vacuolización tubular o "nefrosis osmótica" en pacientes que reciben IGIV por lo que se deben usar con precaución en pacientes con nefritis lúpica con deterioro del filtrado glomerular concomitante y evitar aquellos preparados que contienen sacarosa (33). El uso de IGIV en pacientes con LES y déficits de IgA se asocia a reacciones anafilácticas graves. La frecuencia del déficit de IgA en pacientes con LES es de un 5 a 6% y claramente es más frecuente que en la población general (34). Excepcionalmente se reportó meningitis aséptica (35), y la incidencia de transfusión related acute lung injury (TRALI) en pacientes con enfermedades autoinmunes es desconocido.

La frecuencia de uso de IGIV en HAD no supera al 39% en las diferentes series (11,12,15). La evidencia del uso de IGIV proviene de un solo estudio retrospectivo (11) y de reportes de casos. Shent et al (11) no encontró diferencias estadísticamente significativas entre pacientes que sobrevivieron a un episodio de HAD y aquellos que no, con respecto al uso de IGIV, sin embargo, el diseño de este estudio no permite sacar conclusiones adecuadas. El protocolo que se usa con más frecuencia en la práctica clínica implica una infusión de IGIV en dosis altas, que consiste en una cantidad total de 2 g/kg de peso corporal, generalmente dividida en cinco dosis diarias de 400 mg/kg (7) para minimizar el riesgo de eventos adversos. Las IGIV deberían considerarse en monoterapia o asociados a GC en aquellos pacientes con enfermedad activa a pesar del SOC (6,7) o en aquellos que tengan concomitantemente trombocitopenia (6,7), pseudoobstrucción intestinal (7), compromiso neurológico como neuropatía periférica refractarias (7,30), que cursen embarazo, infección concomitante que contraindique el inmunosupresor (6,7) o historia previa de hipogammaglobulinemia primaria.

RTX es un anticuerpo monoclonal quimérico con acción anti CD20. Hay reportes sobre el uso de RTX con dos dosis intravenosas de 1 gramo separadas entre sí por 14 días (8,36), así como terapia "multitarget" con RTX y CF (27) o RTX con IGIV (37). RTX podría además ser útil en casos de HAD recurrente (13, 37,38).

Se ha descripto el uso de factor VII recombinante activado en HAD refractaria (7,39).

El soporte ventilatorio no difiere del paciente con SDRA y se ha reportado mejorías con modos limitados por presión tales como Airway pressure release ventilation (APRV) (40), y en caso de insuficiencia respiratoria hipoxémica refractaria con insuficiencia cardíaca aguda grave podría recurrirse a la oxigenación por membrana extracorpórea (ECMO) proporcionando tiempo adicional para que actúen los inmunosupresores (41).

Micofenolato de mofetil (MFM) es un inmunosupresor con acción inhibitoria de la síntesis de purinas, después de lograr la remisión de la HAD, el MMF es una opción para mantenerla (7).

Tratamiento Recomendado De La Had

HAD grave	GC +/- pulsos + CyC y/o RTX y/o IGIV y/o PF
HAD refractaria	PF o IGIV o RTX +/- ECMO +/- factor VIIr
HAD recurrente	GC + RTX
HAD en remisión	MFM

III. CONCLUSIONES

La HAD es una complicación potencialmente mortal del LES, y afortunadamente infrecuente. Puede ser la forma de presentación del LES, frecuentemente asociada a nefritis. El tratamiento de la HAD requiere un manejo multidisciplinario y debe hacerse tan pronto se confirme el diagnóstico. El SOC consiste en el uso de glucocorticoides e inmunosupresores. En casos refractarios debe considerarse el uso de PF, IGIV y RTX.

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Use of 3D Cups in Severe Acetabular Defects

Ignacio Troncoso, Gonzalo J. Blanco O´dena & Carlos Sabatella

ABSTRACT

Introduction: Given the increase in hip arthroplasties in the last century, serious acetabular defects are increasingly frequent events. Its treatment represents a real challenge, due to the deficit and poor bone quality, which these patients usually have.

Materials and Methods: Six patients treated between 2016 and 2021 are presented. Five cases of pelvic disruption due to failed revisions, classified as Paprosky type IIIB, and one transverse fracture of the acetabulum, a possible treatment option in cases of osteoporotic patients.

Results: The patients treated with this multidisciplinary technique were followed up for an average of 20 months, none of them presented postoperative complications. The results evaluated by analogous scales are promising and invite us to establish this procedure as the gold standard.

Keywords: pelvic disruption; 3D cup; double mobility; reconstructive acetabular revision; severe acetabular defects.

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Use of 3D Cups in Severe Acetabular Defects

Utilización De Cotilos 3D en Defectos Acetabulares Graves

Ignacio Troncoso[α], Gonzalo J. Blanco O´dena[σ] & Carlos Sabatella[ρ]

RESUMEN

Introducción: Ante el aumento de las artroplastias de cadera en el último siglo, los defectos acetabulares graves son eventos cada vez más frecuentes. Su tratamiento representa un verdadero desafío, debido al déficit y pobre calidad ósea, con la que cuentan habitualmente estos pacientes.

Materiales y Métodos: Se presentan 6 pacientes tratados entre 2016 y 2021. Cinco casos de disrupción pélvica por revisiones fallidas, clasificadas como tipo IIIB de Paprosky y una fractura transversal de acetábulo, posible opción de tratamiento en casos de pacientes osteoporóticos.

Resultados: Los pacientes tratados con esta técnica multidisciplinaria fueron seguidos durante un promedio de 20 meses, ninguno presentó complicaciones postoperatorias. Los resultados valorados por escalas análogas son prometedores e invitan a establecer éste procedimiento como el estándar de oro.

Conclusiones: La evaluación estricta es necesaria en los defectos acetabulares. La inclusión de ingeniería informática médica permite fabricar implantes a medida de titanio/tantalio trabecular multiporoso, lo que es ideal para lograr la osteointegración, sumado a la posibilidad de planificar dirección y longitud de tornillos al hueso remanente, según su calidad.

La cementación de un cotilo de doble movilidad, dentro del implante customizado, disminuye el riesgo de luxación y de sobrecarga de este último, al eliminar la fricción metal-metal.

Palabras clave: Disrupción pélvica; cotilo 3D; doble movilidad; revisión acetabular reconstructiva; defectos acetabulares graves.

ABSTRACT

Introduction: Given the increase in hip arthroplasties in the last century, serious acetabular defects are increasingly frequent events. Its treatment represents a real challenge, due to the deficit and poor bone quality, which these patients usually have.

Materials and Methods: Six patients treated between 2016 and 2021 are presented. Five cases of pelvic disruption due to failed revisions, classified as Paprosky type IIIB, and one transverse fracture of the acetabulum, a possible treatment option in cases of osteoporotic patients.

Results: The patients treated with this multidisciplinary technique were followed up for an average of 20 months, none of them presented postoperative complications. The results evaluated by analogous scales are promising and invite us to establish this procedure as the gold standard.

Conclusions: Strict evaluation is necessary in acetabular defects. The inclusion of medical informatics engineering makes it possible to manufacture custom-made multiporous trabecular titanium/tantalum implants, which is ideal for achieving osseointegration, added to the possibility of planning the direction and length of screws to the remaining bone, according to its quality. Cementing a double mobility cup inside the customized implant reduces the risk of

dislocation and overloading of the latter, by eliminating metal-metal friction.

Keywords: pelvic disruption; 3D cup; double mobility; reconstructive acetabular revision; severe acetabular defects.

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Conflicto de intereses: No contamos con conflicto de interés.

I. INTRODUCCIÓN

La artroplastia de cadera es una de las cirugías más exitosas del siglo XX, ya que permite aliviar el dolor, corregir deformidades y mejorar la función articular.

El componente acetabular fallido es un escenario frecuente y complejo al cual se enfrenta el cirujano de cadera. La mayoría de los fracasos ocurren por aflojamiento aséptico, pero otras posibles causas son: infección, luxación recidivante, fractura periprotésica, incompatibilidad de los componentes, desgaste y osteólisis.

La revisión se ha convertido en un reto, debido a la pérdida de tejido óseo y de su calidad. La dificultad en la reconstrucción se relaciona con identificar la localización y la característica del hueso viable residual. Una vez identificado el patrón del defecto óseo mediante análisis radiográfico, su estadificación facilita la apropiada elección del tratamiento.

Paprosky clasificó los defectos acetabulares en tres tipos. Nos centraremos en el tipo III que se subclasifica en IIIA, y se caracteriza por una migración superior del componente femoral de más de 3 cm, lisis moderada de la imagen en lágrima y línea de Kohler indemne; a diferencia del tipo IIIB que típicamente presenta una migración medial que causa una disrupción de la línea de Kohler, asociada a lisis severa de la imagen en lágrima y el isquion.[1] En nuestra serie, incluimos la descripción de una fractura de acetábulo en un anciano.

Algunas de las técnicas más utilizadas para solucionar estos defectos óseos graves son el uso de aloinjerto estructural en bloque, las mallas antiprotrusión y los implantes a medida. A propósito de las mallas antiprotrusión, se han publicado fallas mecánicas con tasas de hasta el 15% en un seguimiento a mediano plazo, además de neuropraxia del nervio ciático, pérdida de la fijación del implante y fractura de la aleta de fijación. La reconstrucción acetabular con aloinjerto estructural logra resultados variables, con tasas de falla mecánico de hasta el 70% del componente y migración.[2]

Las elevadas tasas de fracaso generaron la necesidad de desarrollar nuevos implantes con propiedades biológicas y mecánicas potenciadas.

Ante esta problemática, se despliega una técnica capaz de analizar, en detalle, el defecto y reconstruir el acetábulo mediante un implante hecho a medida, con titanio trabecular, que encuadre en la anatomía remanente, con el fin de conseguir la estabilidad del implante y devolver la funcionalidad de la articulación.[3]

El objetivo de este estudio fue realizar una investigación bibliográfica sobre las características de la revisión acetabular con componentes 3D a medida, asociados a la cementación del cotilo de doble movilidad, sus resultados funcionales y radiográficos, a propósito de los casos tratados en nuestro hospital, por defecto tipo IIIB de Paprosky y fractura de acetábulo.

II. MATERIALES Y MÉTODOS

Entre 2016 y 2021, se trataron cinco casos de disrupción pélvica por revisiones fallidas, clasificadas como tipo IIIB de Paprosky y una fractura transversal de acetábulo.

Se incluyó a pacientes con reconstrucciones acetabulares fallidas y defectos óseos de tal magnitud que el uso de los métodos clásicos, como injertos o cajas antiprotrusión, estaba descartado. La edad promedio de los pacientes era de 75.3 años y el seguimiento promedio lleva 20 meses (continúa en la actualidad).

En las entrevistas preoperatorias, se aplicaron el *Harris Hip Score* y la escala de evaluación de Merle d'Aubigné y Postel.[3,4]

De acuerdo con el protocolo, se toman radiografías de frente panorámico de ambas caderas, de entrada y salida pélvica, alar y obturatriz (Figura 1A, C, E, G, H, I, K).

Posteriormente se efectúa una tomografía computarizada con cortes de 1-2 mm de toda la pelvis. Las imágenes se analizan con un programa para representarlo de forma tridimensional.

El siguiente paso consiste en calcular la pérdida radial ósea acetabular: se realiza mediante un método computarizado que utiliza la tomografía computarizada procesando la imagen y generando una reconstrucción anatómica 3D.[5] Esta reconstrucción permite estudiar la densidad y la calidad del tejido óseo remanente y, de esta manera, determinar el soporte óseo del implante por crear. Además, se programan la dirección y la longitud de los tornillos de fijación a los sectores del isquion, ilion y pubis que se utilizarán, teniendo en cuenta la calidad de ósea y su posible amarre.

Se trata de un trabajo interdisciplinario, durante el cual el cirujano realiza un constante intercambio con los ingenieros informáticos, enfocado especialmente en optimizar la inclinación, la anteversión y la determinación del centro de rotación (Figura 2).

En todos los casos, se emplea el abordaje posterolateral y se revisa el componente femoral.

Luego de una cuidadosa liberación y disección de las partes blandas, se expone el defecto acetabular que se rellena con injerto óseo siempre proveniente de banco de huesos; de esta manera, se evita la comorbilidad de la toma de injerto de cresta ilíaca, aportando estructura ósea al déficit.

Durante la cirugía, se provee al cirujano de un molde anatómico de prueba, los monitores 3D permiten ubicar el defecto, la posición del componente a medida, los tornillos por colocar, la longitud y la dirección (Figura 3).

El material utilizado para la construcción de los cotilos a medida siempre fue titanio trabecular, debido a su alto coeficiente de fricción que permite brindar estabilidad primaria inicial y, posteriormente, debido a su alta porosidad tridimensional, osteointegración y fijación biológica secundaria (Figura 4).[2,6,7]

A continuación, en el acetábulo a medida, se cementa un cotilo de doble movilidad que aumenta el cociente cabeza-cuello y establece dos superficies articulares brindando mayor estabilidad, evitando la sobrecarga del implante acetabular 3D y disminuyendo el desgaste focalizado del revestimiento de polietileno entrecruzado (Figura 5).

El cotilo de doble movilidad tiene un uso importante en pacientes con alto riesgo de luxación, por ejemplo, aquellos sometidos a cirugías de resección oncológica,[8] con patología cadera-columna o artrodesis lumbosacra previa,[9] con fracturas intracapsulares[10] y los casos de revisiones como los planteados en este estudio.[11] Es necesario un abanico glúteo indemne; si está afectado, se sugiere usar un cotilo constreñido. En todos los casos, se corroboró la correcta longitud y la movilidad articular, y se realizó la reinserción del abanico glúteo.

III. RESULTADOS

El tiempo de hospitalización promedio fue de tres días y la evolución clínico-quirúrgica de los pacientes fue buena. A seis de ellos, se les indicó carga 24 h después de la cirugía, asistida por andador, complementada con ejercicios de movilidad activo-pasiva y fortalecimiento muscular. Al recibir el alta, se prescribieron medidas antiluxación, tratamiento fisiokinésico, analgésicos y anticoagulación/agregación según correspondiera.

El primer control se realizó a las tres semanas de la cirugía y, en ese momento, se retiraron las suturas mecánicas dada la buena evolución de la herida quirúrgica. Se mantuvieron las medidas preventivas de luxación hasta la próxima consulta.

Los siguientes controles se realizaron con radiografías a las 6 semanas, los 2 y 3 meses, y se

indicó el retiro del andador y carga con bastón canadiense. Al sexto mes, se retiró la asistencia para carga de peso y se establecieron controles cada seis meses (Figura 1B, D, F, H, J, L). Hasta el momento, no se han registrado complicaciones posoperatorias.

IV. DISCUSIÓN

El manejo del déficit masivo óseo acetabular es un complejo escenario en la revisión de cadera. La forma de tratar dicho defecto es un tema de controversia; los múltiples procedimientos descritos, como el uso de cotilos de gran tamaño ("Jumbo"),[12] injertos estructurales[13] o celdas de reconstrucción,[14] entre otros, no consiguieron resultados favorables a largo plazo.

Por otro lado, los implantes acetabulares fabricados a medida tienen la ventaja de brindar estabilidad a estos grandes defectos, al mismo tiempo, que permiten complementar el uso de injerto óseo con la expectativa de la fijación biológica.

Christie y cols. controlaron durante 53 meses a 67 pacientes tratados con implantes 3D. El Harris Hip Score mejoró de 33 antes de la cirugía a 82 al final del seguimiento. Los autores afirman que no fue necesaria la revisión en ningún caso; sin embargo, la principal complicación fue la inestabilidad y la luxación de la prótesis.[15]

Por otra parte, Holt y Dennis publicaron datos de 26 pacientes con déficit tipo IIIB de Paprosky. El Harris Hip Score mejoró de 39 a 78 y la tasa de éxito fue del 88%. Tres pacientes presentaron aflojamiento aséptico debido a falla en la fijación por los tornillos isquiáticos y dos, por luxaciones tratadas de forma cerrada.[16]

Joshi y cols. llevaron a cabo una revisión de 27 pacientes con una evolución promedio de 2.3 a 5.3 años, según el puntaje de Charnley modificado de Merle d'Aubigné y Postel. Describen la gran complejidad del procedimiento, pero menos luxaciones a partir de incluir la revisión femoral en todos los casos.[17]

Por último, Wind y cols. publicaron una revisión retrospectiva de 19 pacientes tratados por déficit acetabular tipos IIIA y B de Paprosky, cinco de ellos sufrieron luxación de la prótesis. El 65% de los casos fue considerado exitoso, resultados poco favorables en esta serie de casos, de acuerdo con los autores.[18]

Según lo publicado, la luxación de la prótesis es una de las posibles y frecuentes complicaciones del tratamiento de los defectos acetabulares mediante implantes 3D, además del aflojamiento.

Ante esta situación, el uso de cotilos de doble movilidad, como se describe en esta serie de pacientes, permitirá disminuir la sobrecarga del implante a medida, brindará mayor rango de movilidad, menor desgaste del polietileno y disminuirá el riesgo de luxación de la prótesis, unas de las principales complicaciones descritas en la bibliografía.

El tratamiento de defectos óseos acetabulares tipos IIIA y B de Paprosky se ha convertido en un verdadero desafío en las cirugías de revisión de reemplazos totales de cadera.

En la bibliografía, históricamente, se describen altas tasas de complicaciones, sobre todo de aflojamiento, en los resultados de la reconstrucción de estos defectos masivos mediante técnicas clásicas, como el uso de cotilos de gran tamaño ("Jumbo"), injertos óseos o celdas de reconstrucción, entre otros.

El manejo de este cuadro mediante implantes 3D, creados con ingeniería informática como asistencia, han fundado un nuevo paradigma. Se caracteriza por ser un procedimiento que requiere más tiempo de estudio en cada caso, planificación preoperatoria y alta demanda técnica. Los resultados publicados son alentadores, pues prácticamente elimina los aflojamientos típicos de otros tipos de procedimientos. Sin embargo, la inestabilidad se ha convertido en su principal complicación.

A partir de esta problemática, es que se implementa la cementación de cotilos de doble movilidad en los implantes 3D, eliminando prácticamente los riesgos de inestabilidad y, a su vez, disminuyendo la sobrecarga. La bibliografía internacional al respecto es mínima. Baauw y cols.

Publicaron una serie de 12 casos con un seguimiento mínimo de 18 meses. Ninguno de los pacientes presentó aflojamiento y solo uno sufrió una luxación, en el cual no se había revisado el vástago femoral.

En la Argentina, también, es escasa la bibliografía, se conoce el estudio de Belzino y cols., de 2020.[19] La principal limitación de este estudio es la restringida serie de casos, atribuible directamente al hecho de que es un cuadro infrecuente. La estandarización y agilización de este método terapéutico revisten vital importancia ante el aumento exponencial de las artroplastias de cadera en el mundo, como posible resolución en casos de progresión catastrófica.

V. CONCLUSIONES

Este artículo describe un detallado abordaje del análisis realizado por el equipo de cadera y sus asesores en ingeniería médica informática para elaborar un implante de titanio a medida que permita colocar óptimos anclajes óseos con tornillos en las zonas de mayor amarre, según el tejido óseo remanente particular de cada paciente y el uso de la cementación de cotilos de doble movilidad para disminuir la incidencia de inestabilidad, principal complicación en el tratamiento de defectos acetabulares tipos IIIA y B de Paprosky, con implantes a medida.

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Figura 1: Radiografías de cadera de frente y de perfil, preoperatorias de los casos tratados. A y B. Caso 1. C y D. Caso 2. E y F. Caso 3. G y H. Caso 4. I y J. Caso 5. K y L. Caso 7. La descripción de cada paciente se detalla en la Tabla 1.

Figura 2: Representación y planificación 3D del cotilo tridimensional y los tornillos de fijación ejemplificativos.

Figura 3: Ejemplo de molde para la planificación preoperatoria y el molde utilizado en la cirugía del Caso 1.

Figura 4: Imagen intraoperatoria del cotilo tridimensional utilizado como restrictor; permite, a su vez, rellenar espacios y dar fijación biológica por su elaboración en tantalio (Caso 3).

Figura 5: Imagen intraoperatoria de la cementación del cotilo de doble modularidad dentro del implante tridimensional. Esto permite disminuir la sobrecarga sobre este último y disminuir los riesgos de luxación, una de las complicaciones más frecuentes cuando se utiliza el cotilo 3D.

Tabla: Descripción de los seis casos tratados con implantes 3d y cotilo de doble movilidad

Pacientes/ sexo/edad	Motivo de la revisión	Clasificación de Paprosky	Número de revisión	Revisión del vástago	Uso de injerto	HHS pre quirúrgico	Puntaje de Merled' Aubigne'y Postel pre quirúrgico	Complicaciones hasta la fecha	HHS posquirúrgico	Puntaje de Merled' Aubigne'y Postel posquirúrgico
1/F/45	Aflojamiento aséptico	IIIB	1	Sí	Sí	39	7	X	87	15
2/F/76	Aflojamiento séptico	IIIB	3	Sí	Sí	29	4	X	80	13
3/F/84	Aflojamiento aséptico	IIIB	1	Sí	Sí	23	3	X	91	17
4/M/92	Aflojamiento séptico	IIIB	3	Sí	Sí	22	4	X	78	12
5/M/82	Aflojamiento aséptico	IIIB	1	Sí	Sí	21	3	X	83	14
6/F/73	Fractura acetábulo	X	X	X	Sí	X	X	X	86	15

M = masculino, F = femenino, HHS = Harris Hip Score