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Implications of increasing pollution levels on commercially important fishes in Lake Victoria

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ABSTRACT

Lake Victoria receives huge quantities of effluent from domestic, agricultural and industrial sources. We used fish condition factor (K), vitellogenin (VTG) production and liver lesions as biomarkers to assess pollution levels in the lake. We tested the hypothesis that pollution levels do not affect the selected biomarkers. Beach seine and cast nets were used to collect *Oreochromis niloticus* (n = 230), *Lates niloticus* (n = 99) and *Protopterus aethiopicus* (n = 37) in areas presumed to be less or more polluted, both inshore and offshore. K was lower in more polluted compared to less polluted areas of the lake. VTG production was high in both less and more polluted areas for *O. niloticus* (0.77 ± 0.08 μg/L), *L. niloticus* (0.73 ± 0.09 μg/L) and *P. aethiopicus* (0.55 ± 0.06 μg/L). Liver tissue showed lesions such as vacuolations, cellular degeneration, sinusoidal dilation, focal necrosis, increased Küpffer cells and congestion of sinusoids. The prevalence of liver tissue alteration showed normal lesion (19.9%, n = 73), slight (8.2%, n = 30), moderate (41.5%, n = 152), severe (18.6%, n = 68) alterations and irreparable damage (11.8%, n = 43). Severe liver alterations in *O. niloticus, L. niloticus* and *P. aethiopicus* were higher in more polluted compared to less polluted areas. Chemical contamination of Lake Victoria caused liver lesions and other changes in fishes, possibly leading to adverse effects on the lake's fisheries resources. Overtime, such chemical contamination could lead to negative impacts on the consumers of fish if actions are not taken to mitigate the risks.

Introduction

Up to the middle of the 20th century, the Lake Victoria ecosystem consisted of over 500 endemic fish species, of which 60% belonged to the cichlids (Aloo et al., 2017). The fishes of Lake Victoria have diverse life histories, with several key species contributing to its important fishery. Nile tilapia (*Oreochromis niloticus*) live in tropical freshwater bodies and tolerate environmental fluctuations. As an omnivorous species, its food selection depends on the season, maturity and prevailing environmental conditions. In the Lake Victoria fishery, *O. niloticus* is of high economic importance, second to Nile perch (*Lates niloticus*) (Gu et al., 2018). *L. niloticus* matures at the age of three years, and their predatory feeding habit make them eat their own juveniles (Yongo et al., 2017). In Lake Victoria, marbled lungfish (*Protopterus aethiopicus*) inhabit mainly shallow inshore waters, dense vegetation zones, such as papyrus swamps (Goudswaard et al., 2002a,b). The fish aestivates in swampy mud, where they stay in cocoons made from clay, and undergo metabolic depression for several months. *Protopterus aethiopicus* are omnivorous, feeding mainly on plant materials, insects and crustaceans (Yasindi, 2013). During spawning seasons, they construct nests by digging pits on the lake bottom. The eggs are laid within the nests, where males guard them, as well as the young (Mlewa and Green, 2004; Ishimatsu et al., 2018). Other species of commercial importance in the lake include *Barbus, Clarias, Labeo, Synodontis and Rastrineobola argentea*. However, 1979–1990 data on the catches of fisheries of Lake Victoria showed drastic decrease to extremely low levels of over 80 species of the cichlids (Goudswaard et al., 2002a,b; Aloo et al., 2017). Decline in fish biodiversity in the lake is mainly attributable to the fishing pressure and introduction of the predatory *L. niloticus* in the 1950s (Witte et al., 1992; Aloo et al., 2017). Further, anthropogenic and industrial wastes caused hypoxia, eutrophication and deterioration of water quality, resulting in extinction of several fish species in Lake Victoria (Kaufman, 1992; van Rijssel et al., 2017; van den Thillart et al., 2018).

The Ugandan portion of Lake Victoria receives huge quantities of either raw or poorly treated effluent from domestic, industrial and pharmaceutical sources, especially from Kampala, Entebbe and Jinja towns. Further, runoff and leachate carry agro-pesticides used on flower farms, sugar cane and tea estates in the catchment into

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the lake. Municipalities and towns in Uganda have low sewerage coverage, estimated at 6.4% despite high effluent volumes and loads (NWSC, 2009). Whereas Uganda's National Environmental Management Authority requires that industries operate effluent treatment plants (ETPs) that meet stringent discharge limits (NEMA, 1999), many release untreated wastes into the environment. On the other hand, industries that have ETPs use technologies that do not efficiently remove all contaminants, hence discharge poorly treated effluents into rivers or catchment areas that drain into Lake Victoria (Matagi, 2002; Odong et al., 2013). Further, due to the high annual human population growth rate of 3.3% (UBOS, 2007), the highest globally (Hartter et al., 2015), vast acreages of lacustrine wetlands of Lake Victoria have either been converted for settlement, industries, agriculture, roads, or seriously degraded to the extent that they can no longer perform natural buffering and bioremediation functions (Kansiime and Maimuna, 1999; Kyambadde et al., 2004; Odong et al., 2015).

The Nakivubo Wetland receives channelized streams conveying wastewater from industrial and residential areas of Kampala, Uganda's largest city. to Murchison Bay, Lake Victoria near Kampala city. Previous studies in areas of high human activities, i.e. Port Bell, Ggaba, Kasenyi and Jinja towns showed high levels of cadmium (0.14 mg/L), copper (3.3 mg/L) and iron (21.5 mg/L) in water samples of the lake (Fuhrimann et al., 2015). Further studies have shown heavy metal contamination, i.e. zinc (Zn), lead (Pb), copper (Cu) and nickel (Ni) in Lake Victoria wetlands (Nabulo et al., 2008). Also, agro-pesticides, for example, dieldrin, aldrin, dichlorodiphenyltrichloroethane (DDT) were reported in the lake water (Wasswa et al., 2011). Mercury (Hg) and cadmium (Cd) have been found in fish tissue (Hollamby et al., 2004; Focardi et al., 2006), while the agro-pesticides dichlorodiphenyldichloroethane (DDD), and DDT were found in fish blood plasma of Lake Victoria (Ogwok et al., 2009). On the basis of threshold effect concentration to freshwater sediment-dwelling organisms (1.9 μg/kg), according to the International Programme on Chemical Safety, aldrin and dieldrin pose the most serious threats to the lake (Wasswa et al., 2011). Both aldrin and dieldrin are poisonous to fish and fish consumers due to their effects on the liver, causing morbidities and mortalities (Younes, 2000). Several cardiovascular and endocrine diseases that affect human health are associated with consumption of Hg contaminated fish (Mozaffarian and Rimm, 2006). Further, polychlorinated biphenyls (PCBs) and dioxin in fish cause fatty liver, diabetes and cancer among regular fish consumers (Al-Eryani et al., 2015). Meanwhile, consumption of fish contaminated with DDT is associated with neurological malfunction and impairment of cognitive development in infants and adults (Bernstein et al., 2019). The accepted limit of 0.5 mg/kg of Hg in fish (Gaudet et al., 1995), and a monthly intake not exceeding 0.07 ng/kg of dioxin are both considered safe for human consumption according to FAO and WHO (Malisch and Kotz, 2014).

Fish may ingest heavy metal and pesticide contaminants in food items, or absorb them from suspended particulate matter through their respiratory gills, causing oxidative stress (Demeke and Tassew, 2016; Gautam et al., 2016). When fish liver receive poisonous environmental chemicals through the gastrointestinal tract, they perform important roles of oxidative defence, detoxification and xenobiotics excretion (Wolf and Wheeler, 2018). Further, the liver is the site where the VTG molecule is synthesized and conveyed to oocytes for growth and development. Liver histopathological alterations are reported as biomarkers of the effect of exposure to environmental contaminants, hence used for pollution monitoring in aquatic environments (Al-Zaidan et al., 2015; Bhuvaneshwari et al., 2015; Diamond et al., 2016). Indeed, exposure of fish to contaminants have been shown to induce liver lesions (Abdel-Moneim, 2014; Feist et al., 2015; Abdel-Moneim et al., 2016). Also, categories of liver lesion (non-specific, toxicopathic non-neoplastic, pre-neoplastic and neoplastic) can be assigned following evaluation of biological effects of contaminants in fishes (Lang et al., 2006). Chemical environmental contaminants induce VTG molecule production by liver cells (Hara et al., 2016; Louiz et al., 2018; Okihiro et al., 2018; Tolussi et al., 2018; Van Veld et al., 2018; Wolf and Wheeler, 2018). Studies on fish liver have shown foci of cellular alterations, hepatocellular adenoma and degenerative lesions (Feist et al., 2005; Feist et al., 2015). Severe toxicopathic netpen liver lesions in Atlantic salmon (*Salmo salar*) characterised by melano-macrophage, diffuse hydropic degeneration and necrosis, most likely attributable to algal toxins have been reported (Kent, 1990). Further, fishes, for example zebrafish (*Danio rerio*), medaka (*Oryzias latipes*), and fathead minnow (*Pimephales promelas*), are used as sentinel for assessing toxicity of contaminants in aquatic environment through exposure to respiratory, dermal and digestive routes (Wolf and Wheeler, 2018). In polluted Egyptian lakes, *O. niloticus* showed necrosis, melanomacrophage infiltration, congestions, pyknosis, and vacuolation corresponding to the relatively high lipid content (Abdel-Moneim et al., 2016). Liver diseases caused by exposure of fish to chemical contaminants affecting metabolism and storage of fats also reduce liver body mass index and general condition factor (K). Because K represents fish health in relation to general physiology and metabolic processes, it also reflects feeding conditions and energy conversion in the body. Therefore, a high level of chemical contaminants in the water can impact the liver and K negatively. Several studies from around the world recommend use of liver histopathological alterations in health evaluation of both experimental and wild fish populations (Schwaiger et al., 1997; Figueiredo-Fernandes et al., 2007; Liu et al., 2007; Dias et al., 2014; Feist et al., 2015). The usefulness of using K in monitoring overall wellbeing of fish and contamination of aquatic environment is supported by Ebeh et al. (2017).

Despite high levels of environmental contaminants, for example heavy metals, organochlorine pesticides and PCBs in Lake Victoria, Uganda (Wasswa et al., 2011; Ssebugere et al., 2014b), prior to this study, there were no reported studies of possible fish liver histopathological alterations. The present study aimed to find whether *L. niloticus*, *O. niloticus*, and *P. aethiopicus* from the lake, exposed to chemical environmental contaminants, suffer from liver histopathological alterations, altered VTG production and poor K, as observed in fishes elsewhere. We did this by collecting fish from various regions of the lake and then comparing between polluted and less polluted areas. We tested the hypothesis that pollution levels do not affect the biomarkers of fish.

Materials and methods

Lake Victoria is shared among three countries, Tanzania (51% of lake area), Uganda (43%) and Kenya (6%). Globally it is the second largest lake covering 68,000 km^2, with a catchment area of 193,000 km^2 (Nyammeya, et al., 2016). The Lake Victoria region is among the most densely populated areas in Africa with over 35 million people living in its catchment near the shores (LVEMP, 2018). In the Ugandan catchment around the urban areas at Port Bell, Ggaba, Kasenyi and Jinja, there are high human settlements and industries (e.g. tanneries, pharmaceuticals, plastics and fish processing) that release chemical contaminants through streams, ending in Lake Victoria. To test the hypothesis that pollution levels do not affect selected biomarkers of fishes, our sampling sites in the lake were located both inshore (<1km from shores) and offshore (>1km away from shores) around the more polluted areas of Jinja, Port Bell, Kasenyi and Ggaba, while less polluted areas receiving mainly agricultural wastes were used for reference (Table 1). The areas studied are parts of the towns or districts of

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Table 1
Description of fish sampling sites along Lake Victoria, Uganda from the western part of River Kagera, Rakai district to the eastern Kirinya wetlands, Jinja (*less polluted areas due to less human impacts, **more polluted areas due to higher human impacts).

Sampling site	Co-ordinate	Description
Kasensero*	00°54′53′′ N, 31° 45′47′′E	1.5 km away from River Kagera confluence that received into Lake Victoria discoloration biomass of planktonic debris
Baale*	00°32′52¨N, 31° 48′45′′E	40 km from Masaka agricultural field, and *Eucalyptus* plantations where the lake received fertilizers and agrochemicals
Bukakkata*	00°18′16′′ N, 32° 02′19′′E	44 km east of Masaka town on the western shores of the lake which received agrochemicals from nearby rice field
Kasenyi**	00°15′ 56¨ N, 32° 37′08′′E	5.5 km off Entebbe road at Abaita Ababiri where the lake received copious waste from poultry, piggery and fish farms
Ggaba**	00°15′21¨ N, 32° 37′59′′E	Adjacent to the urban area of the city of Kampala from which the lake received numerous pollutants from urban waste
Port Bell**	00°17′53′′ N, 32° 39′11′′E	11 km south-east Kampala city centre, industrial area, at narrow inlet of the lake that received large a volume of waste
Jinja**	00°27′52′′N, 33° 14′16′′E	Adjacent Kirinya ETP, behind wetland near Jinja prison at industrial areas that discharged untreated sewage to the lake

Kampala, Wakiso, Jinja, Masaka and Rakai in the Lake Victoria catchment of Uganda (Fig. 1). A description of each sampling site categorised as less polluted and more polluted is presented (Table 1). At the Kasensero site in Rakai district, large biomasses of debris of plants enter the lake through River Kagera. The Victoria Nile in the northern part of Jinja is the only outlet of the lake. The sites were selected based on land use practices, i.e. agriculture, industries and urban settlements, fishing villages, effluent discharge and population density. Site selection also considered previous findings (Supplementary Data) and reports on toxic environmental contaminants in water, sediment and fish tissues (Banadda et al., 2011; Wasswa et al., 2011; Kerebba et al., 2017).

Fish sampling was conducted fortnightly, beginning September 2016 to August 2017 from seven sites spread along Ugandan portion of Lake Victoria from the western district of Rakai, to the eastern, Jinja (Fig. 1). Sampling was done with the help of local fishermen using a combination of fishing gears, including seine, cast, and gill nets to catch representative fish species at different sizes and growth stages. A total of 366 fish specimens were collected alive, with at least 20 caught per trip for efficient handling and processing. The fish specimens collected were handled based on ethical guidelines for animals (Grigorakis, 2010; Bergqvist and Gunnarsson, 2013). Fishes collected were carefully immersed in cold buckets containing distilled water (20L) to avoid causing suffocation and pain. Prior to the hypothermia condition, we immersed fish specimens in a water bath containing clove oil as a sedative. Fish were killed with a soft blow to the head (Shoko et al., 2015). Fish were weighed to the nearest 0.1 g body mass (BM), while total length (TL), distance from the tip of the snout to the tip of the caudal fin were measured to the nearest 1 cm as described by Feist et al. (2015). Samples were wrapped in ice packed-chilled buckets and transported to the Department of Zoology, Entomology and Fisheries Sciences, Makerere University for further processing.

Sample processing

Blood samples were collected using syringes from fish caudal veins and injected into clotting activator vacutainer tubes (serum separating red tops) and kept in a vertical position overnight at room temperature. The following day, the samples were centrifuged for 15 min at 1300 rpm. Thereafter, serum was collected

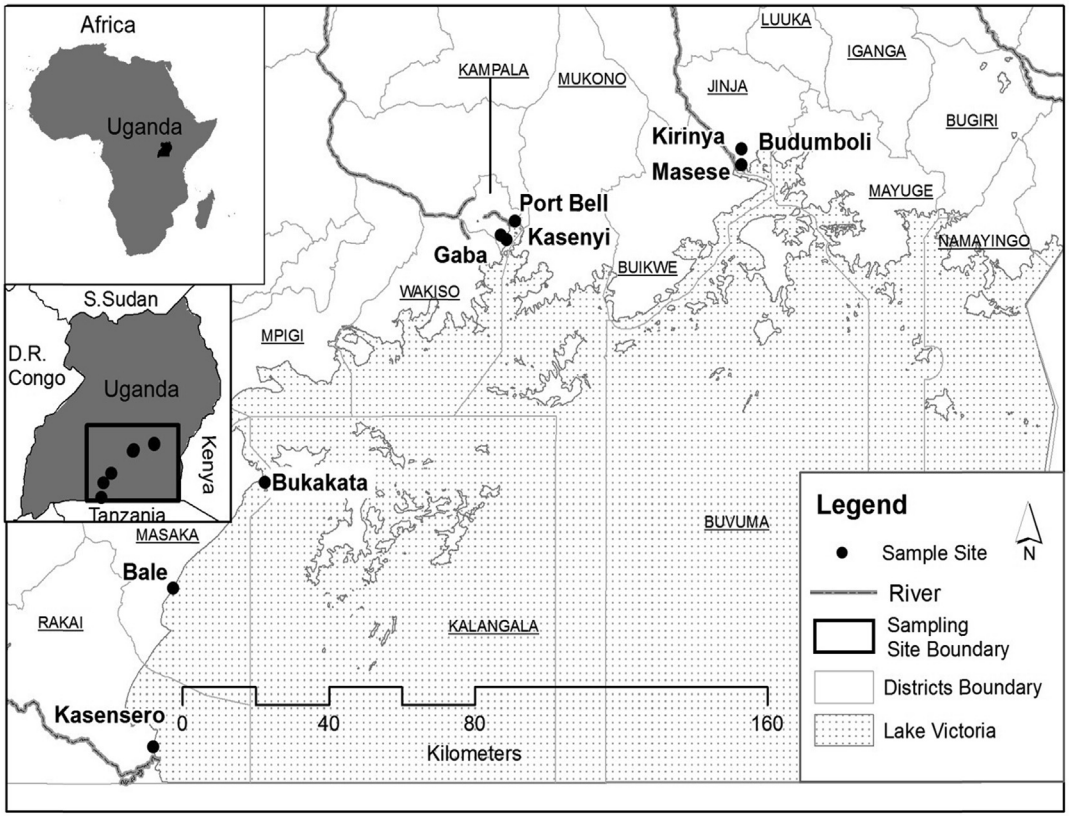

Fig. 1. Study area, from the western district of Rakai to eastern Jinja, Lake Victoria, Uganda from where fishes were sampled.

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into cryovial tubes, quickly frozen, and stored at −40 °C or less, until assayed for VTG. The viscera cavity was split open to harvest the liver and gonads, followed by weighing to the nearest 0.01g. The sex of fish samples and gonadal development stages were determined by visual inspection as described by Nandikeswari (2016).

In larger fish specimens, standardized 3–5 mm sections of the liver were harvested from the anterior, posterior and middle for histopathology examination. Prior to histological examination, the samples were fixed in 10% neutral buffered formalin for 48 h coupled with agitation to ensure thorough fixation of specimens. The fixed specimens were transferred into 70% industrial methylated spirit and transported to the Histology Laboratory at the College of Veterinary Medicine, Animal Resources and Biosecurity, Makerere University for histological analyses. The samples were dehydrated in a series of ethanol, cleared in xylene, impregnated with paraffin in a vacuum infiltration processor, and embedded into wax blocks. Similarly, standardized 3–5 μm microtome sections of the liver tissue were subjected to normal routine of haematoxylin and eosin (H&E) stains (Barnhoorn et al., 2010). To establish diagnosis correctly, the prepared slides were analysed using light microscope (Nikon Eclipse E800), first using the lowest power objective lens (X 10) and then higher magnification (X 40). To capture the liver images, the binocular light microscope (Nikon Eclipse Ci-S) was connected to television screen, where focusing for good resolution was done. The filmstrip was used to scroll between images, while the magnification slider selected the resolution corresponding to the objective lenses of a light microscope. Detailed information of the images captured are displayed on the status bar.

Calculation of biometric indices

Hepatosomatic index (HSI) was obtained by using the liver mass (g) / body mass (g) × 100 (Nunes et al., 2011). Fulton condition factor (K) of individual species were calculated using the equation; $K = 100 \times W/TL^3$; W = body mass (g), TL = total length (cm) (Agbohessi et al., 2015).

VTG measurement in blood serum

Quantitative Sandwich enzyme-linked immunosorbent assay (ELISA) developed by My BioSource Laboratory, kit Cat. No: MBS010726 was used for detection of VTG in fish blood serum. The sensitivity of the kit was 5.0 ng/mL, with detection range of 31.2 to 1000 ng/mL, and intra/inter-coefficient variability of <15%. The presence and concentration of VTG were determined in undiluted serum collected from fish samples. The 96 wells of the microtiter plates were pre-coated with captured antibodies that bound with VTG in standards and samples added to the wells. Each of the six standard wells received 50 μL of the standard solution (1000, 500, 250, 125, 62.5, 31.2 ng/mL), which were expected to cover a range of target analytes in undiluted samples according to the manufacturers.

To each sample well, 50 μL of the serum was added while, 50 μL of sample diluent was added to the control well, a volume (100 μL) of horseradish peroxidase-conjugate reagent was added into each well (standard, sample, and control). Thereafter, the plate was covered with closure plate membrane and incubated at 37 °C for 60 min. After incubation, the analyte was washed four times with a washing solution and cleaned using absorbent papers until no moisture remained. A 50 μL volume of chromogen solutions A and B was pipetted and introduced into each well successively, and then mixed gently away from sunlight. The mixture was incubated at 37 °C for 15 min. To the mixture in each well, a volume of 50 μL stop solution was introduced, and positive results developed with change of colour from blue to yellow. For optical density, an ELISA reader at 450 nm was used, and the value obtained corresponded with the quantity of VTG in each fish serum sample.

Histopathological alterations in fish liver

Fish liver was screened for the degree of altered features, and assessed semi-quantitatively to predict the chemical contaminant levels of sampling points and the lake generally. The severity of alteration were ranked to score value; i.e. Stage 0 = no alteration; Stage 1 = minimal alterations, infection does not alter tissue functions (for example cytoplasmic vacuolation and proliferation of hepatopancreas): Stage 2 = moderate alterations, infection impair normal tissue functions (e.g. degeneration of the cytoplasm and nuclei); Stage 3 = severe alterations lead to irreparable damage of tissues, resulting in tumours and fibrosis (Lukin et al., 2011; Paulo et al., 2012). The degree of tissue alteration (DTA) was calculated for each fish using the formula: DTA = (1 × Si) + (10 × Sii) + (100 × Siii); where; i, ii, and iii correspond to the number of alterations in stages 1, 2, and 3 respectively. The value of S represents the sum of alterations in a given stage (Paulo et al., 2012; Dane and Sisman, 2017). Further, liver histopathological alterations for each fish was assigned a DTA score and categorized as: 0 to 10 = normal liver tissue, 11 to 20 = slight alterations of the tissue, 21 to 50 = moderate changes in the tissue, 51 to 100 = severe lesions in the liver tissue, 101 and above = irreversible damage in the liver tissue as described elsewhere (Lukin et al., 2011; Paulo et al., 2012; Dane and Sisman, 2017).

Data analysis

Statistics software (IBM SPSS, Statistics 20, and STATA (R), version 13.0) were used for analyses. The normality of biometrical data was assessed using the Kolmogorov-Smirnov test. The intensity of fish liver tissue alterations among fish species and sampling sites were tested by one-way ANOVA followed by Tukey's post hoc tests. Descriptive statistics presented percentage prevalence, means, and standard deviations. Non-parametric Mann-Whitney *U* test and Kruskal-Wallis followed by pairwise comparisons were used for detection of differences in mean values of liver alterations among fish species, sampling sites and seasons. The association of biomarkers on fish length was analysed using Pearson correlation analysis.

Results

Condition factor

A total of 366 fish specimens were collected, which comprised of 230*O. niloticus* (100-females, 130-males), 99 *L. niloticus* (50 males, 49 females), and 37*P. aethiopicus* (22 males, 14 females, and 1 intersex). Fish lengths for *O. niloticus* (TL > 22 cm), *L. niloticus* (TL > 30 cm) and *P. aethiopicus* (TL > 55 cm) dominated the population structure of the sampled populations (Fig. 2). Mean values of K were for *O. niloticus* (1.91 ± 0.02 SE), *L. niloticus* (1.61 ± 0.10 SE), and *P. aethiopicus* (0.70 ± 0.11 SE). Kruskal-Wallis test showed significant difference in K of all fish species ($p < 0.001$). The highest peak of K was recorded during rainy months for *O. niloticus* ($F_{(1, 228)} = 11.342$, $p < 0.05$), *L. niloticus* ($F_{(1, 97)} = 0.036$, $p > 0.05$), *P. aethiopicus* ($F_{(1, 35)} = 1.634$, $p > 0.05$). Also, K differed significantly between less and more polluted areas, ANOVA ($F_{(6, 223)} = 5.58$, $p < 0.001$), ($F_{(6, 92)} = 10.12$, $p < 0.001$) and ($F_{(5, 31)} = 2.76$, $p < 0.05$) for *O. niloticus, L. niloticus* and *P. aethiopicus* respectively (Table 2). Further, Tukey's HSD post hoc test, showed that less polluted areas had higher K compared to the more polluted areas (Bukakkata = Kasensero > Ggaba = Jinja). We found significantly different K among

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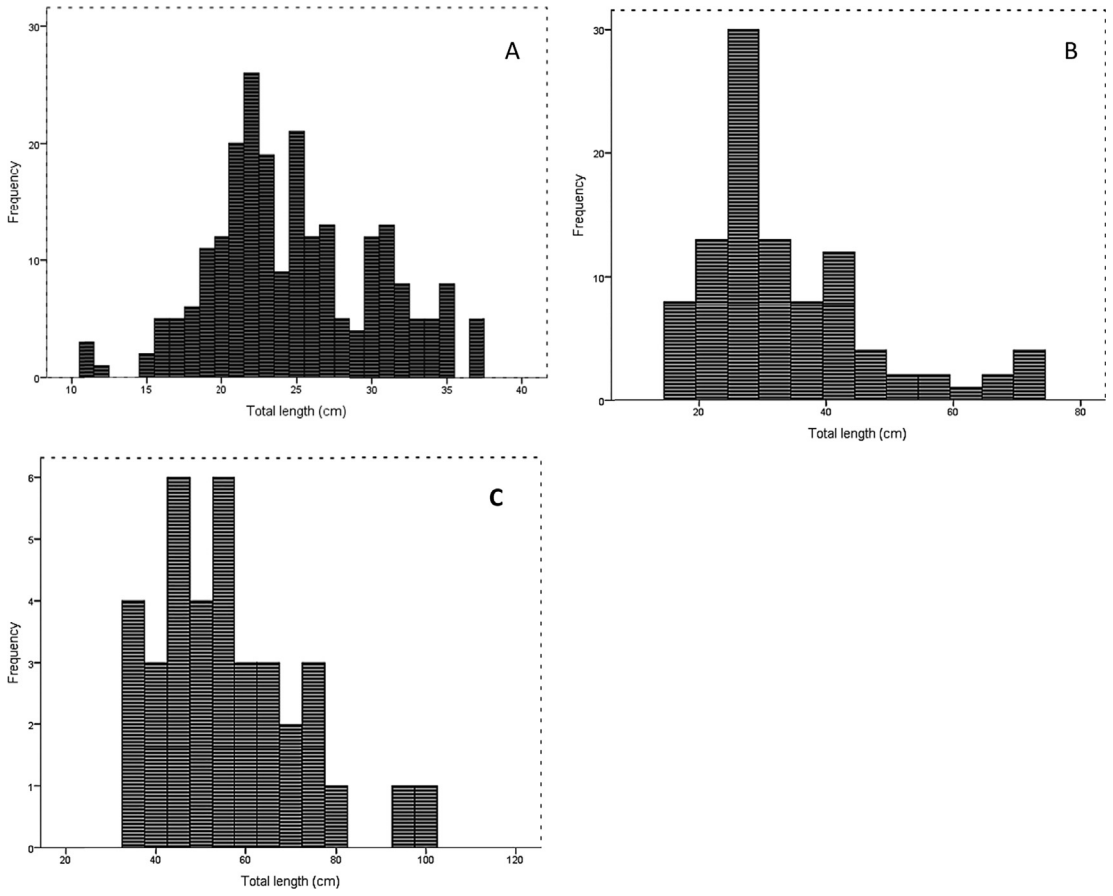

Fig. 2. (A, B and C) Length-frequency distribution of *Oreochromis niloticus*, *Lates niloticus* and *Protopterus aethiopicus* respectively, from Lake Victoria, Uganda.

Table 2
Distribution of samples and their mean and standard deviation (in parentheses) for some key biological factors for *O. niloticus, L. niloticus, and P. aethiopicus* between less polluted and more polluted areas of Lake Victoria, Uganda (- specimens were not found, *p-value < = 0.05, ** p-value < = 0.01, liver DTA scores; 0 to 10 = normal liver tissue, 11 to 20 = slight alterations, 21 to 50 = moderate changes, 51 to 100 = severe lesions, 101 and above = irreversible damage of the liver tissue).

Bio. factor/ Species	Less polluted areas (Rural)				highly polluted areas (Urban)					Average urban
	Kasensero	Baale	Bukakkata	Mean	Kasenyi	Ggaba	Port Bell	Jinja	Mean	
Condition factor										
*O. niloticus**	7(1.8 ± 0.3)	18(1.7 ± 0.3)	39(1.9 ± 0.2)	64(1.8 ± 0.3)	54(2.0 ± 0.3)	40(1.8 ± 0.3)	39(1.9 ± 0.2)	33(2.0 ± 0.3)	166(1.9 ± 0.3)	
*L. niloticus**	9(1.8 ± 0.6)	14(2.4 ± 1.3)	15(1.1 ± 0.4)	38(1.8 ± 0.8)	14(1.4 ± 0.9)	15(1.5 ± 0.2)	13(2.7 ± 1.3)	19(1.0 ± 0.5)	61(1.6 ± 0.7)	
*P. aethiopicus**	4(1.1 ± 0.3)	2(0.4 ± 0.1)	3(1.6 ± 0.1)	9(1.0 ± 0.2)	–	11(0.3 ± 0.1)	10(0.7 ± 0.8)	7(0.8 ± 0.9)	28(0.6 ± 0.6)	
Hepatosomatic index										
*O. niloticus**	7(1.7 ± 0.4)	18(1.6 ± 0.4)	39(1.2 ± 0.4)	64(1.5 ± 0.4)	54(1.1 ± 0.6)	40(1.2 ± 0.5)	39(1.2 ± 0.5)	33(1.2 ± 0.6)	166(1.2 ± 0.6)	
*L. niloticus**	9(2.2 ± 0.5)	14(1.6 ± 0.7)	15(1.4 ± 0.6)	38(1.7 ± 0.6)	14(1.4 ± 0.7)	15(1.2 ± 0.4)	13(1.3 ± 1.5)	19(1.2 ± 0.6)	61(1.3 ± 0.8)	
*P. aethiopicus**	4(1.6 ± 0.7)	2(2.1 ± 0.2)	3(0.9 ± 0.1)	9(1.5 ± 0.3)	–	11(2.0 ± 0.5)	10(1.4 ± 0.5)	7(1.7 ± 0.5)	28(1.7 ± 0.5)	
Vitellogenin (μg/L)										
*O. niloticus**	6(0.5 ± 0.3)	5(0.6 ± 0.5)	8(0.2 ± 0.1)	19(0.4 ± 0.3)	9(0.5 ± 0.3)	8(1.2 ± 0.3)	8(1.5 ± 0.5)	8(0.8 ± 0.4)	33(1.0 ± 0.4)	
*L. niloticus**	3(0.5 ± 0.2)	2(0.4 ± 0.0)	3(0.6 ± 0.3)	8(0.5 ± 0.2)	1(0.6 ± 0.0)	2(1.5 ± 0.2)	2(0.7 ± 0.4)	3(0.8 ± 0.1)	8(0.9 ± 0.2)	
*P. aethiopicus***	–	1(0.5 ± 0.0)	–	1(0.5 ± 0.0)	1(0.7 ± 0.0)	–	–	2(0.5 ± 0.1)	3(0.6 ± 0.0)	
Liver DTA scores										
*O. niloticus**	7(26 ± 23)	18(47 ± 68)	39(27 ± 23)	64(33 ± 38)	54(59 ± 69)	40(53 ± 71)	39(91 ± 87)	33(102 ± 146)	166(76 ± 93)	
*L. niloticus**	9(29 ± 21)	14(37 ± 94)	15(21 ± 25)	38(29 ± 47)	14(44 ± 56)	15(78 ± 107)	13(34 ± 24)	19(39 ± 53)	61(48 ± 60)	
*P. aethiopicus**	4(19 ± 14)	2(411 ± 271)	3(14 ± 12)	9(145 ± 99)	–	11(96 ± 127)	10(95 ± 181)	7(44 ± 136)	28(78 ± 148)	

sexes inhabiting less and more polluted areas of the lake. Among *L. niloticus* and *P. aethiopicus,* females in less polluted areas had higher K than those in more polluted areas. Among *O. niloticus* and *L. niloticus* (Fig. 3), males exhibited lower K in less polluted than polluted areas. The inshore and offshore areas showed no significant differences in K for *O. niloticus* ($F_{(1,\ 228)} = 0.396$, $p > 0.05$), *L. niloticus* ($F_{(1,\ 97)} = 0.052$, $p > 0.05$), and *P. aethiopicus* ($F_{(1,\ 35)} = 9.460$, $p > 0.05$). We observed no significant difference ($p > 0.05$) in K among the three fish species for categories of liver abnormalities. However, among the sexes in *P. aethiopicus* and *L. niloticus* with liver abnormalities, K showed significant differences. The mean value of K according to maturity stages was highest in *O. niloticus* (1.91 ± 0.29, n = 230). However, lower K values in *P. aethiopicus* (0.70 ± 0.68, n = 37) and *L. niloticus* (1.61 ± 1.01, n = 99) were observed. The value of K in fish decreased as the body size increased, for *O. niloticus* ($r = -0.444$, $p < 0.001$), *L. niloticus*

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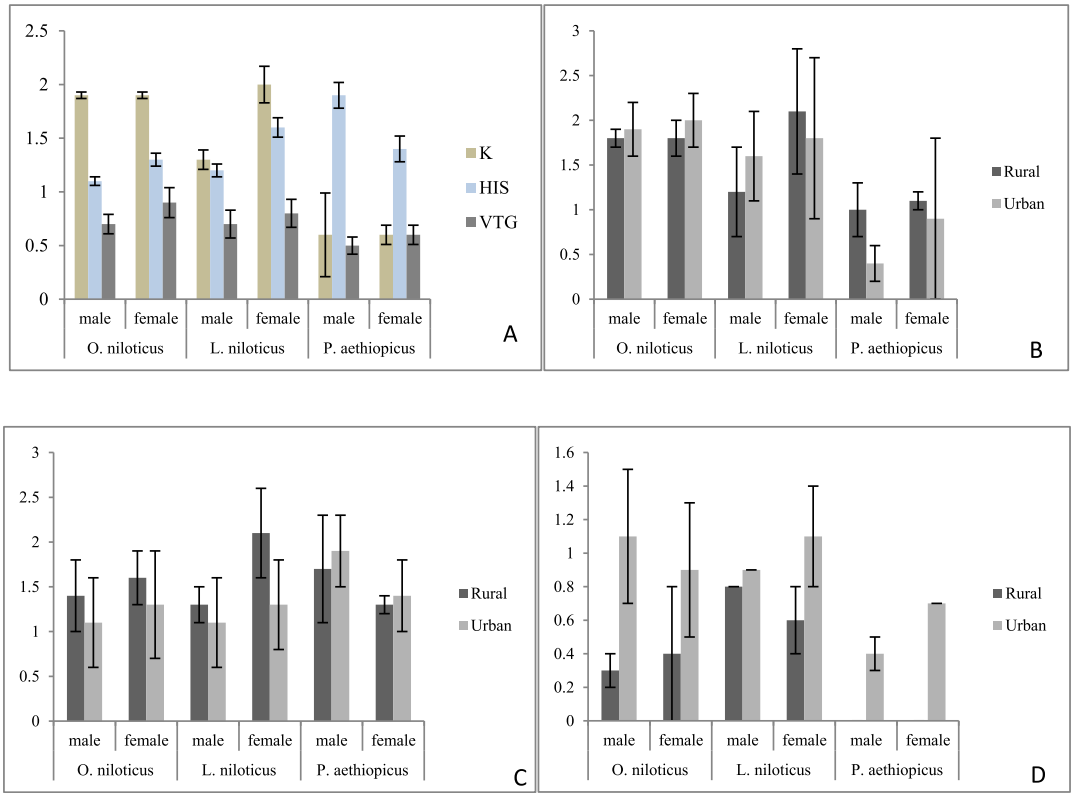

Fig. 3. A = mean values of condition factor (K), hepatosomatic index (HSI) and vitellogenin (VTG) among sexes for *O. niloticus*, *L. niloticus* and *P. aethiopicus* in Lake Victoria, Uganda. B = mean value of K among male and female fish species in less polluted (rural) and more polluted areas (urban). C = mean value of HSI among male and female fish species in less polluted and more polluted areas. D = mean value of VTG among male and female fish species in less polluted and more polluted areas of the lake.

(r = -0.630, p < 0.001), *P. aethiopicus* (r = -0.595, p < 0.001). Larger fish would likely have had higher and longer level of exposure and bio-accumulation of contaminants in the lake, and consequently a lower K value.

Hepatosomatic index

Exposure of fish to chemical substances reduce the rate of liver metabolic activities. For example, it reduces the secretion of enzymes that break down fats, decreases storage of fats, and lessen energy reserves, hence resulting in reduced liver body mass index. The average hepatosomatic index (HSI) value for *O. niloticus* (1.21 ± 0.03), *L. niloticus* (1.41 ± 0.06), and *P. aethiopicus* (1.65 ± 0.09) showed significant differences among the three fish species (p < 0.001). However, Tukey's HSD post hoc test showed no significant difference of HSI between *L. niloticus* and *P. aethiopicus* (p > 0.05). The mean value of HSI for male (1.12 ± 0.04, n = 130) and female (1.34 ± 0.06, n = 100) *O. niloticus* were recorded, with significant differences between the sexes. Results of the study showed the highest HSI in *L. niloticus* throughout the sampling period. The values of HSI were different among less and more polluted areas, ANOVA ($F_{(6, 223)} = 4.11$, $p < 0.05$), ($F_{(6, 92)} = 5.28$, $p < 0.001$) and ($F_{(5, 31)} = 3.23$, $p < 0.05$) for *O. niloticus, L. niloticus* and *P. aethiopicus* respectively (Table 2). Further, Tukey's HSD post hoc test, results showed that less polluted areas had higher HSI compared to the more polluted areas (Bukakkata = Kasensero > Ggaba = Jinja, Kasenyi = Port Bell). Among the less and more polluted areas, higher HSI were found in females compared to males. Further, results showed higher HSI in females from less polluted compared to those in more polluted areas. Similarly, higher HSI in males from less polluted areas compared to those inhabiting more polluted areas was observed (Fig. 3). The polluted and non-polluted regions showed no significant differences in HSI for *O. niloticus* ($F_{(1, 228)} = 1.155$, $p > 0.05$) and *L. niloticus* and ($F_{(1, 97)} = 1.532$, $p > 0.05$). We observed no significant difference in HSI values among the species and sexes for categories of liver lesions ($P > 0.05$). Indeed, highest HSI values among maturity stages in *P. aethiopicus* suggested good condition (Table 3). However, HSI in males and females among the maturity stages were not significantly different. The value of HSI increased with body size for *O. niloticus* (r = 0.069, p > 0.05), while a negative correlation for *L. niloticus* (r = -0.423, p < 0.001) and *P. aethiopicus* (r = -0.035, = p > 0.05) were recorded. The impression for the latter two species is that bio-accumulation of contaminants in larger fish may be higher than in juveniles in chemically contaminated environment due to longer exposure.

VTG production in fish

Normal and mature female fish release estradiol hormone from ovarian follicular cells. The liver synthesizes VTG molecules under the influence of circulating estradiol. However, some chemical pollutants mimic natural estrogens and induce high VTG in male and juvenile fishes. A high level of VTG in *O. niloticus* (0.77 ± 0.08 μg/L, n = 52), *L. niloticus*, (0.73 ± 0.09 μg/L, n = 16) and *P. aethiopicus* (0.55 ± 0.06 μg/L, n = 4) with no significant difference between species was recorded. However, production of VTG showed site-specific significant differences among *O. niloticus* ($F_{(6, 45)} = 13.6$, $p < 0.001$) and *L. niloticus* ($F_{(6, 9)} = 5.67$, $p < 0.05$). In both less and more polluted areas, VTG production were significantly lower in males compared to females among species examined (Fig. 3). Further, Tukey's HSD post hoc tests showed that fishes in more pol-

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Table 3
Sample distribution and their mean and standard deviation in parentheses for key biological parameters for maturity stages of fish species for three fish species observed in Lake Victoria, Uganda (- specimens were not found, *p-value < = 0.05, ** p-value < = 0.01, liver degree of tissue alteration (DTA) scores; 0 to 10 = normal liver, 11 to 20 = slight alterations, 21 to 50 = moderate changes, 51 to 100 = severe lesions, 101 and above = irreversible damage of the liver tissue).

	O. niloticus			***Maturity stages in P. aethiopicus***			***O. niloticus***	
Key biological factor	immature	developing	spawning	spent	I	II	III	IV
Condition factor**	38(1.98 ± 0.39)	59(1.97 ± 0.22)	107(1.88 ± 0.28)	26(1.78 ± 0.26)	50(1.26 ± 0.09)	49(1.98 ± 0.17)	22(0.55 ± 0.39)	15(0.61 ± 0.09)
Hepatosomatic index*	38(1.08 ± 0.47)	59(1.08 ± 0.50)	107(1.27 ± 0.54)	26(1.47 ± 0.26)	50(1.21 ± 0.06)	49(1.61 ± 0.09)	22(1.85 ± 0.12)	15(1.37 ± 0.12)
Vitellogenin * (μg/L)	14(0.54 ± 0.41)	10(0.50 ± 0.37)	19(0.90 ± 0.59)	9(1.18 ± 0.64)	16(0.66 ± 0.13)	7(0.79 ± 0.13)	2(0.49 ± 0.08)	2(0.61 ± 0.09)
Liver DTA scores**	38(65.3 ± 74.5)	59(50.8 ± 65.2)	107(61.4 ± 84.2)	26(86.8 ± 132.4)	50(48.0 ± 10.9)	49(33.4 ± 7.1)	22(83.3 ± 31.1)	15(105.3 ± 39.6)
	L. niloticus			spent	*Maturity stages in P. aethiopicus*			
	immature	developing	spawning		I	II	III	IV
Condition factor*	25(1.73 ± 1.14)	19(1.91 ± 1.13)	45(1.53 ± 0.96)	10(1.14 ± 0.27)	50(1.26 ± 0.09)	49(1.98 ± 0.17)	22(0.55 ± 0.39)	15(0.61 ± 0.09)
Hepatosomatic index**	25(1.48 ± 0.60)	19(1.33 ± 0.63)	45(1.43 ± 0.62)	10(1.27 ± 0.53)	50(1.21 ± 0.06)	49(1.61 ± 0.09)	22(1.85 ± 0.12)	15(1.37 ± 0.12)
Vitellogenin * (μg/L)	1(0.42 ± 0.00)	2(1.05 ± 0.48)	9(0.76 ± 0.39)	4(0.60 ± 0.31)	16(0.66 ± 0.13)	7(0.79 ± 0.13)	2(0.49 ± 0.08)	2(0.61 ± 0.09)
Liver DTA scores**	25(32.9 ± 43.9)	19(41.3 ± 80.2)	45(49.1 ± 73.2)	10(22.4 ± 28.6)	50(48.0 ± 10.9)	49(33.4 ± 7.1)	22(83.3 ± 31.1)	15(105.3 ± 39.6)
	P. aethiopicus			spent	*Maturity stages in P. aethiopicus*			
	immature	developing	spawning		I	II	III	IV
Condition factor*	1(0.29 ± 0.00)	4(0.72 ± 0.55)	25(0.68 ± 0.77)	7(0.85 ± 0.50)	50(1.26 ± 0.09)	49(1.98 ± 0.17)	22(0.55 ± 0.39)	15(0.61 ± 0.09)
Hepatosomatic index**	1(2.62 ± 0.00)	4(1.81 ± 0.56)	25(1.72 ± 0.52)	7(1.19 ± 0.43)	50(1.21 ± 0.06)	49(1.61 ± 0.09)	22(1.85 ± 0.12)	15(1.37 ± 0.12)
Vitellogenin** (μg/L)	- -	- -	3(0.50 ± 0.76)	1(0.70 ± 0.00)	16(0.66 ± 0.13)	7(0.79 ± 0.13)	2(0.49 ± 0.08)	2(0.61 ± 0.09)
Liver DTA scores**	1(22.0 ± 0.0)	4(17.0 ± 15.5)	25(113.0 ± 171.9)	7(49.0 ± 78.3)	50(48.0 ± 10.9)	49(33.4 ± 7.1)	22(83.3 ± 31.1)	15(105.3 ± 39.6)

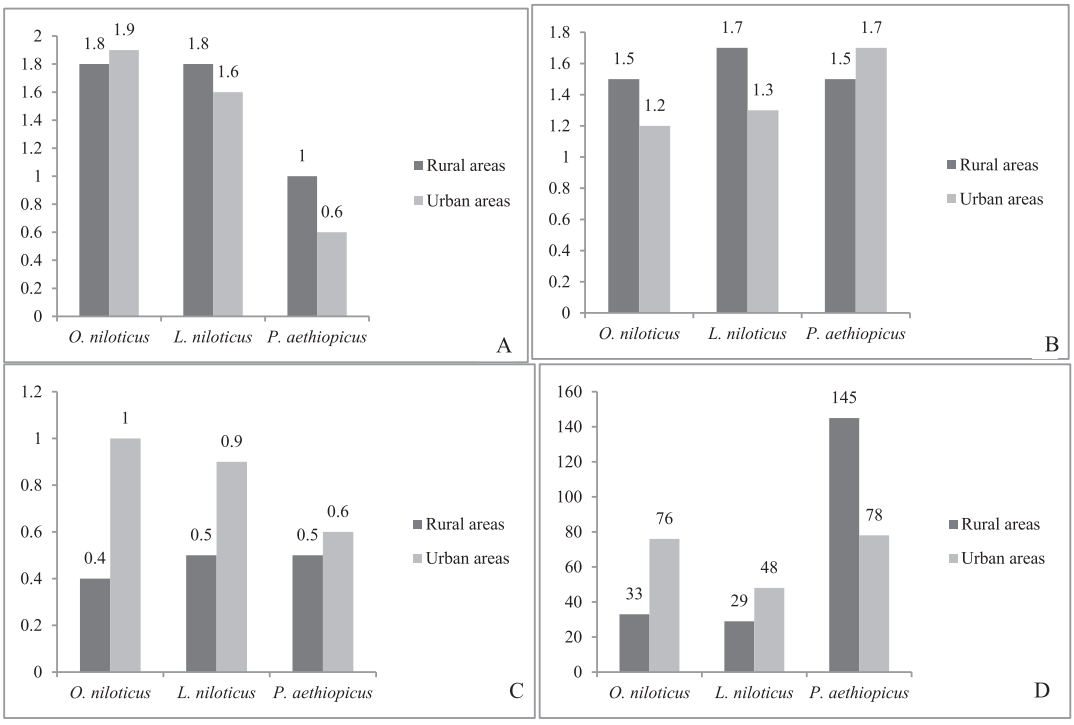

Fig. 4. A = mean value of condition factor (K) among fish species in less polluted (rural) and more polluted areas (urban). B = mean value of hepatosomatic index (HSI) among fish species in less polluted and more polluted areas. C = mean value of vitellogenin (VTG) of fish species in less polluted and more polluted areas. D = mean value of liver degree of tissue alteration (DTA) scores of fish species in less polluted and more polluted areas of Lake Victoria, Uganda (liver DTA scores; 0 to 10 = normal liver tissue, 11 to 20 = slight alterations, 21 to 50 = moderate changes, 51 to 100 = severe lesions, 101 and above = irreversible damage of the liver tissue).

luted areas had higher VTG levels compared to less polluted areas (Jinja = Kasenyi, Ggaba = Ports Bell > Bukakkata = Baale, Kasenseso = Baale) (Fig. 4). For the inshore and offshore, fish samples showed no difference in VTG levels for *O. niloticus* ($F_{(1, 50)} = 0.111$, $p > 0.05$) and *L. niloticus* ($F_{(1, 14)} = 0.084$, $p > 0.05$). We observed higher VTG production in females compared to males in specimens showing categories of liver lesions. Highest level of VTG production among female maturity stages followed the order *O. niloticus* ($F_{(3, 48)} = 4.06$, $p < 0.05$) > *L. niloticus* ($F_{(3, 12)} = 1.32$, $p > 0.05$) > *P. aethiopicus* ($F_{(1, 2)} = 4.97$, $p > 0.05$). However, VTG production in males among the maturity stages was significantly different in *O. niloticus* and *L. niloticus* (Table 3). The value of VTG increased as TL increased for *O. niloticus* ($r = 0.254$, $p > 0.05$) and *P. aethiopicus* ($r = 0.188$, $p > 0.05$), while a negative correlation for *L. niloticus* ($r = -0.074$, $p > 0.05$) were recorded. The pattern of VTG expressed sensitivity of the biomarker in large and juvenile fish exposed to high level of contamination in the lake.

DTA in the liver

In fishes, normal liver hepatocytes are hexagonal, showing clear bile ducts and blood vessels (hepatic artery and portal vein) at the

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portal areas. The appearance of sinusoidal spaces is often converging towards the central vein (Fig. 6). However, the liver samples examined from more polluted areas showed a wide range of lesions including vacuolation, fatty degeneration, cellular hypertrophy, karyorrhexis pyknosis, karyolysis, sinusoidal enlargement, infiltrations of mononuclear lymphocyte and focal necrosis (Fig. 7). Also, increased Küpffer cells, dilated portal area and sinusoidal regions, peripancreatic hepatocyte proliferation and blood congestion (Fig. 8), as described elsewhere (Stentiford et al., 2003; Molavi, 2017) were observed. The islets of exocrine pancreatic tissue were dispersed in the liver (hepatopancreas). In a few liver samples, shapes of the hepatocytes appeared necrotically and lost cellular stainability. In many fish specimens, several liver alterations were observed.

A total of 366 fish liver samples were screened for abnormalities related to different levels of exposure to pollution. Those abnormalities were converted into DTA scores or hepatic alteration index (HAI). A total of 73 samples (19.9%) were observed without abnormalities (DTA score = 0–10). On the individual fish species analysis of DTA scores (Fig. 5), results showed that the liver of *O. niloticus* had the lowest prevalence of 15.6% (normal liver, DTA score 0–10) compared to corresponding alterations observed in *L. niloticus* (28.3%) and *P. aethiopicus* (24.3%). Moderate damage in the liver (DTA score 21–50) was the highest incidence category among all the fish species examined. Also, results of fish liver DTA scores at less and more polluted areas (Table 2) showed moderate to severe alterations as the predominant cases. Significantly higher DTA scores at more polluted compared to low polluted areas in *O. niloticus* ($F_{(6, 223)} = 3.722$, $p < 0.05$), *L. niloticus* ($F_{(6, 92)} = 1.139$, $p < 0.05$) and *P. aethiopicus* ($F_{(5, 31)} = 2.990$, $p < 0.05$) were observed. Preponderance of severe liver cases (DTA scores = 51 to 100) were observed among more polluted areas of Ggaba, Jinja, Port Bell, and Kasenyi compared to less polluted areas of Kasensero and Bukakkata (Table 2). We found that the incidence rate of normal liver (without irregularities) were higher in less polluted compared to more polluted areas in *O. niloticus* (83.3%, n = 12), *L. niloticus* (75.0%, n = 16) and *P. aethiopicus* (50.0%, n = 6) (Table 4). However, fish liver DTA scores inshore, and offshore in each of the less and more polluted areas were not significantly different for *O. niloticus* ($F_{(1, 228)} = 0.677$, $p > 0.05$) and *L. niloticus* ($F_{(1, 97)} = 0.049$, $p > 0.05$). Generally, DTA scores for inshore and offshore regions for the species ($n_{\text{near shore}} = 174$, mean rank = 191.7, $n_{\text{offshore}} = 192$, mean rank = 176.1, U = 18,134, $p > 0.05$) were not significant. Fish liver damage (DTA scores) were different between rainy and dry seasons for *O. niloticus* ($F_{(1, 228)} = 10.907$, $p < 0.05$), *L. niloticus* ($F_{(1, 97)} = 0.510$, $p > 0.05$) and *P. aethiopicus* ($F_{(1, 35)} = 0.577$, $p > 0.05$). The liver DTA scores for *O. niloticus* were higher in the rainy compared to dry seasons, while for *L. niloticus* and *P. aethiopicus*, they were higher during the dry compared to rainy seasons. The fish species showed significant differences between dry and wet seasons (Mann Whitney, $n_{\text{dry season}} = 200$, mean rank = 160.8, $n_{\text{rainy season}} = 166$, mean rank = 210.8, U = 12,076, $p < 0.001$). We observed the largest proportion of *P. aethiopicus* with highest DTA score incidence (113.0 ± 171.9, n = 25) at the spawning stage of development, suggesting poor liver condition (Table 3). However, the DTA scores showed no significant difference among maturity stages in *O. niloticus* ($F_{(3, 226)} = 1.09$, $p > 0.05$), *L. niloticus* ($F_{(3, 95)} = 0.63$, $p > 0.05$) and *P. aethiopicus* ($F_{(3, 33)} = 0.75$, $p > 0.05$). The DTA scores increased with increased body size of fish for *O. niloticus* ($r = 0.124$, $p > 0.05$), *L. niloticus* ($r = 0.089$, $p > 0.05$), and *P. aethiopicus* ($r = 0.150$, $p > 0.05$). This showed that larger fish have higher frequency of severe liver alterations. Therefore, there are potential health effects to humans who consume larger fish from contaminated sites of Lake Victoria.

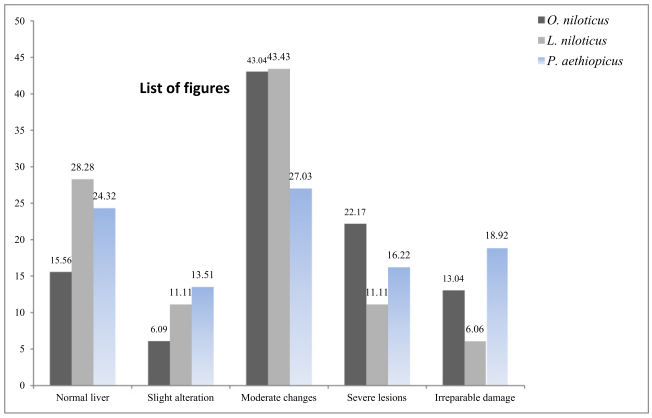

Fig. 5. Proportions of liver based on degree of tissue alteration (DTA) scores observed among *O. niloticus* (n = 230), *L. niloticus* (n = 99) and *P. aethiopicus* (n = 37) in Lake Victoria, Uganda (Liver DTA scores; 0 to 10 = normal liver tissue, 11 to 20 = slight alterations, 21 to 50 = moderate changes, 51 to 100 = severe lesions, 101 and above = irreversible damage of the liver tissue).

Discussion

This study explored the potential implications of increasing pollution on the health of commercially important fish species (*O. niloticus*, *L. niloticus*, and *P. aethiopicus*) in less polluted and more polluted areas of Lake Victoria. The species are of great value because they are consumed at national, regional and international levels. The results not only have implications on the health of the fish species but also on their consumers. Indeed, several studies in the lake have reported chemical contaminants in water, fish tissue and blood. Notably, contaminants like PCBs, dioxin, DDT, endosulfan, lead, arsenic, cadmium and mercury at deleterious concentrations in more polluted areas of Napoleon Gulf (Kenya) and Murchison Bay have been reported (Electronic Supplementary Material (ESM) Table S1). Through consumption of contaminated fish along the food chain, such chemicals biomagnify and pose health risks, notably cancers, physical and birth defects to humans (Jiang et al., 2005; Wang et al., 2005; Alamdar et al., 2017). In monitoring fish health in aquatic environment, liver lesions (for example vacuolation, cellular hypertrophy, and necrosis) and VTG level in males and juveniles are frequently observed (Louiz et al., 2018). In fishes, physiological stress contributes to liver polymorphism (Brusle and Anadon, 1996). Biomonitoring of pollutants using liver lesions has been used in gobies (*Gobius niger*) from the Southern Mediterranean Sea, polluted rivers (Colin et al., 2016; Louiz et al., 2018), and caged fishes in polluted aquatic habitats (Viarengo et al., 2007).

In this study, differences in some key biological factors including K and HSI were evaluated as biomarkers of exposure to chemicals in more polluted and less polluted areas of Lake Victoria, Uganda. We observed that pollution levels affected the selected biomarkers of fishes. Integrative measures of K and HSI provide valuable information concerning the overall effect of pollutants on fish and can be related to both VTG production and level of lesions in the liver. Chellappa et al. (1995) calculated similar indices in male three-spined sticklebacks (*Gasterosteus aculeatus*) from River Kelvin, Glasgow as measures of biochemical composition, predictors of glycogen, protein and lipid in the liver. The three biomarkers studied in fish were at the different levels of organization, i.e. tissue (VTG), organ (liver histopathology) and organismal (K).

Condition factor

In fish health bioassessment, K is a somatic biomarker, which is related to food availability, feeding conditions and energy conversion in the body (Sadauskas-Henrique et al., 2011; Morado

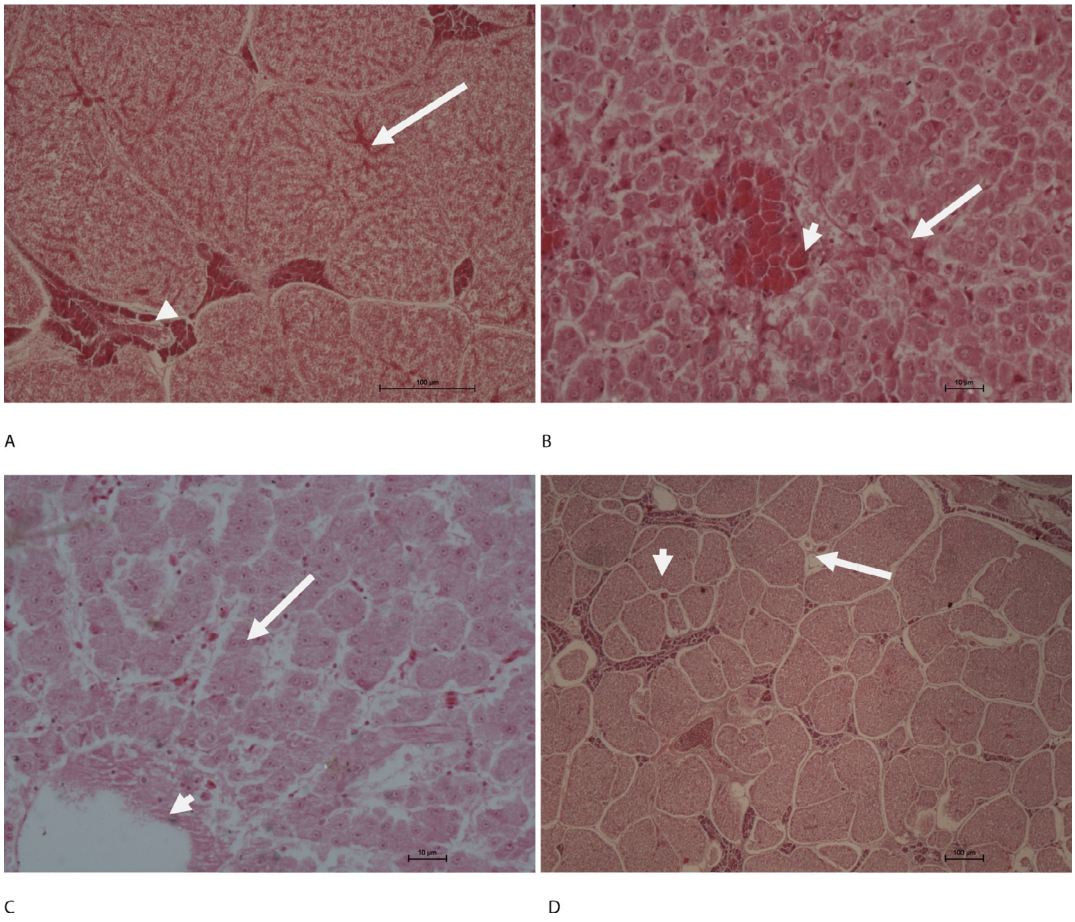

Fig. 6. A-B: Liver histomicrograph of *L. niloticus* from highly polluted areas (urban) at Ggaba showing moderate alteration A = sinusoidal congestion (arrow), scattered hepatopancreas (arrow head) (formalin, H&E, 4X, bars = 100 μm). B = hyperplasia of bile preductular epithelial cells (arrow head), a pyknotic hepatocytes regeneration and scattered vacuoles (arrow) (formalin, H&E, 40X, bars = 10 μm). C-D: Liver histomicrograph of *L. niloticus* from less polluted areas (rural) at Bale, showing normal architecture of the liver cells. C = normal liver cells with central vein (arrow head), sinusoidal regions with basophilic cells (arrow) (formalin, H&E, 40X, bars = 10 μm). D = highly lobulated liver showing clear portal triad (arrow), a clear sinusoidal spaces (arrow head) (formalin, H&E, 4X, bars = 100 μm).

et al., 2017). Therefore, a high level of chemical contaminants in water may impact K negatively, leading to imbalanced physiological function and poor growth of fishes. For example, for three fish species in a tropical river, Southern Brazil, those living in presumably disturbed sites showed lower K compared to those inhabiting less disturbed sites, albeit lower K was also recorded during the dry seasons compared to rainy seasons (Morado et al., 2017). Environmental stressors like Pb, Zn and Cd cause damage to the gills, whereas debris of organic wastes can block the gills surface and hinder oxygen intake for efficient respiration, lowering K (Komjarova and Blust, 2009; Wong et al., 2013). Indeed, other factors rather than the presence of contaminants in the environment including diseases, stress, temperature and seasonality indirectly affect normal growth in fish, hence negatively altering K (Marco-López et al., 2010; Debes et al., 2016).

Generally, higher K values indicate fitness and wellbeing of fish populations (Datta et al., 2013). Mean values of K based on Fulton's interpretation were higher in less polluted compared to highly polluted areas for *L. niloticus* and *P. aethiopicus,* indicating unfavourable condition for fish survival in the more polluted areas. K for *O. niloticus* was higher and fairly uniform among more polluted areas of the lake, probably due to better adaptation to acute hypoxia (Choi et al., 2007). However, based on a scale developed by Barnham and Baxter (2003), overall K values of *O. niloticus* (1.91 ± 0.02 SE), *L. niloticus* (1.61 ± 0.10 SEM), and *P. aethiopicus* (0.70 ± 0.11) in Lake Victoria were excellent, fair, and extremely poor respectively. Lower K value (0.6 to 0.9) was recorded in *Clarias gariepinus* from Gauteng dam, South Africa (Marchand et al., 2009), and hyper-eutrophic freshwater ecosystems in South Africa (Wagenaar and Barnhoorn, 2018), similar to the K value for *P. aethiopicus* in the present study. Brodeur et al. (2000) reported K (0.45–1.20) in walleye pollock fish (*Theragra chalcogramma*) collected off-shore, with a significantly higher K than inshore fishes in the Bering Sea. From results of the present study, sites within the lake receiving industrial and municipal pollutants, e.g. Ggaba had significantly lower K for *L. niloticus* (1.5 ± 0.2) and *P. aethiopicus* (0.3 ± 0.1) compared to less polluted sites, e.g. Baale for *L. niloticus* (2.4 ± 1.3) and *P. aethiopicus* (0.4 ± 0.1). Through omnivorous feeding, *O. niloticus* may feed on harmful algal species and other contaminated aquatic organisms, exposing them to toxins in more polluted areas. previous studies have observed that Ggaba and Port Bell have higher levels of polluting chemicals in water, sediment and fish tissues than low pollution sights (ESM Table S1). The value of K in fish decreased as the body size increased in Lake Victoria. Therefore, a hypothesis based upon our observation that larger fish have higher levels of exposure to contaminants, which lower their K value.. The synergistic effects of contaminants combined with other stressors in the aquatic environment result in poor K, an indication that the environment is potentially under considerable stress.

Vitellogenin induction in the liver

The mean value of VTG was lower in less polluted compared to highly polluted areas, and not significantly different between

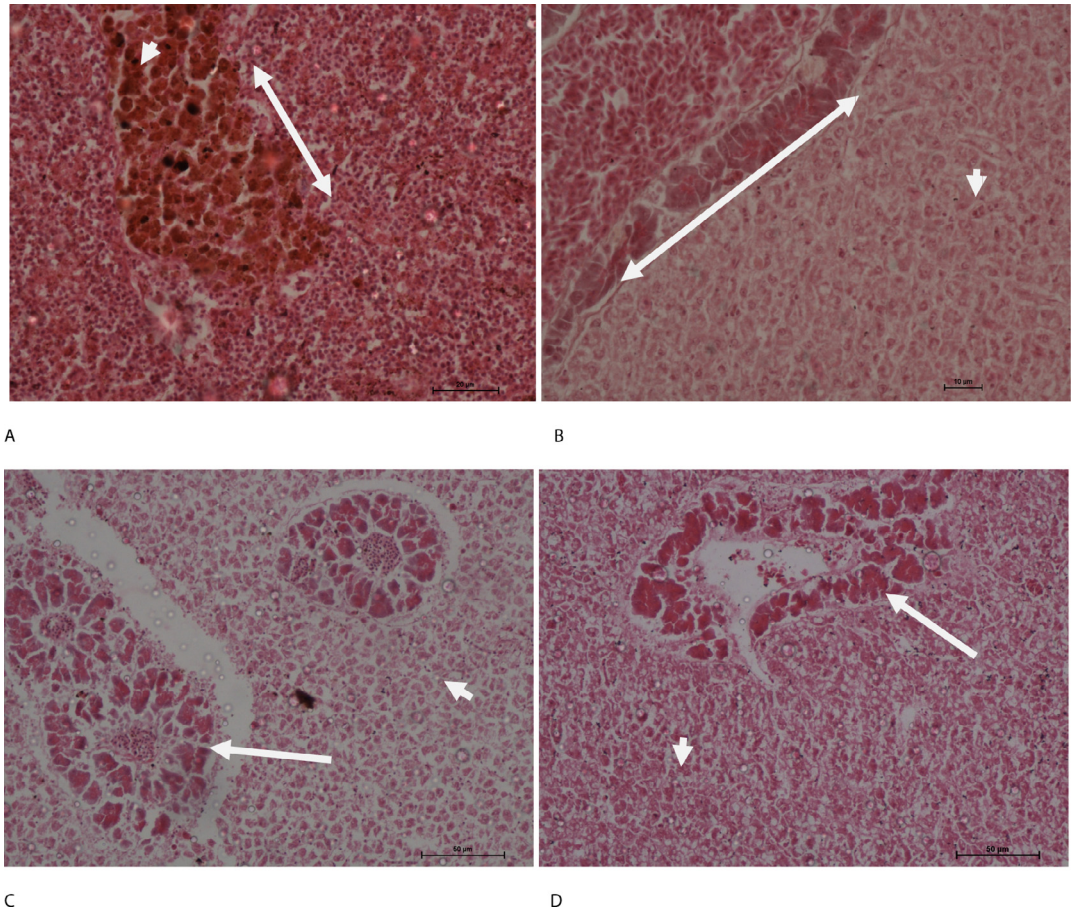

Fig. 7. A-B; Liver histomicrograph of *O. niloticus* with severe alterations from highly polluted areas (urban) at Port Bell. A = multifocal of cellular alteration (two headed arrow) pigment deposits in macrophages (hemosiderin) lipofuschin (arrow head) (formalin, H&E, 40X, bars = 20 μm). B = dilated and congested hepatopancreas (two headed arrow) and liver hapatocytes degeneration (arrow head) (formalin, H&E, 10X, bars = 10 μm). C-D: Liver histomicrograph of *O. niloticus* with minimal alteration from less polluted areas (rural) at Bukakkata. C = diffuse vacuolations in liver (arrow head), dilated hepatopancreas liver (arrow) (formalin, H&E, 20X, bars = 60 μm). D = multifocal perivascular exocrine cell growth (arrow), moderate diffuse hydropic vacuolations (arrow heads) (formalin, H&E, 20X, bars = 50 μm).

species and sexes. Under normal conditions, the gene for the synthesis of VTG in males is turned off. We found that the quantity of VTG in the serum among fish species correlated positively with liver weight. However, VTG were induced abnormally among male fishes from more polluted sites, indicating increasing pollution level where urban runoff may deliver estrogenic contaminants to the lake. At a concentration of 0.1 ng l^{-1}, 17α-ethinylestradiol induced VTG production in male *O. mykiss* (Labadie and Budzinski, 2005). When VTG in the serum of wild male flounders (*Pleuronectes yokohamae*) was investigated as biomarkers for environmental chemicals in contaminated aquatic environment, results showed high levels of VTG (Hashimoto et al., 2000). Further, Meng et al. (2017) reported increased level of VTG in the serum of male *O. niloticus* exposed to chemical contaminants (methomyl) at sub-lethal concentrations (20, and 200 μg/L). Indeed, in comparison, VTG is considered to be a better biomarker following the order VTG > estradiol (E_2) > Testosterone (T) > 11-ketotestosterone (11-KT) (Meng et al., 2017). Occurrence of elevated VTG levels in fish raise concerns, because it affects their reproductive ability and success. Moreover, high levels of VTG contributes to losses of calcium and subsequently scales, exposing bare fish skins to high risk of harm due to parasitic and bacterial infections (Parker and McKeown, 1987; Gross-Sorokin et al., 2006). When long-term exposure to environmental concentrations of ethinylestradiol was tested on *Danio rerio* fish, the F_1 males showed reduced VTG response compared to F_0 (Nash et al., 2004). Also, when adult male medaka fish (*Oryzias latipes*) were exposed to 4-*tert*-octylphenol (xenoestrogens), VTG levels in serum increased (Gronen et al., 1999). The value of VTG increased as TL of fish increased in less and more contaminated areas of the lake, with a positive correlation for *O. niloticus* and *P. aethiopicus*. This pattern of VTG levels showed sensitivity of the biomarker in detecting exposure to estrogenic contamination. However, larger fish have higher VTG production, indicating a possible health risk on their consumers, especially from more polluted areas of the lake.

Liver lesions in fish

Fish liver is composed of 60% hepatocytes (parenchymal cells), and 30% non-parenchymal cells (Küpffer, stellate and endothelial cells) with endocrine and exocrine functions (Nguyen-Lefebvre and Horuzsko, 2015). Liver lesions infer chronic exposure of fish to pollutants in aquatic environments (Louiz et al., 2018). Several researchers recommend liver lesions as biomarkers or histological tools for ecosystem health assessments, especially for wild fish populations. As biomarkers, liver lesions have the advantage of potentially integrating effects of pathogens, temperature fluctuations and chemicals (Zimmerli et al., 2007). However, owing to the diverse nature of chemicals, ascertaining cause-effect relationships of specific contaminants on liver tissue lesions of wild fish species is problematic. Nonetheless, several qualitative observations of histopathological lesions have been converted into

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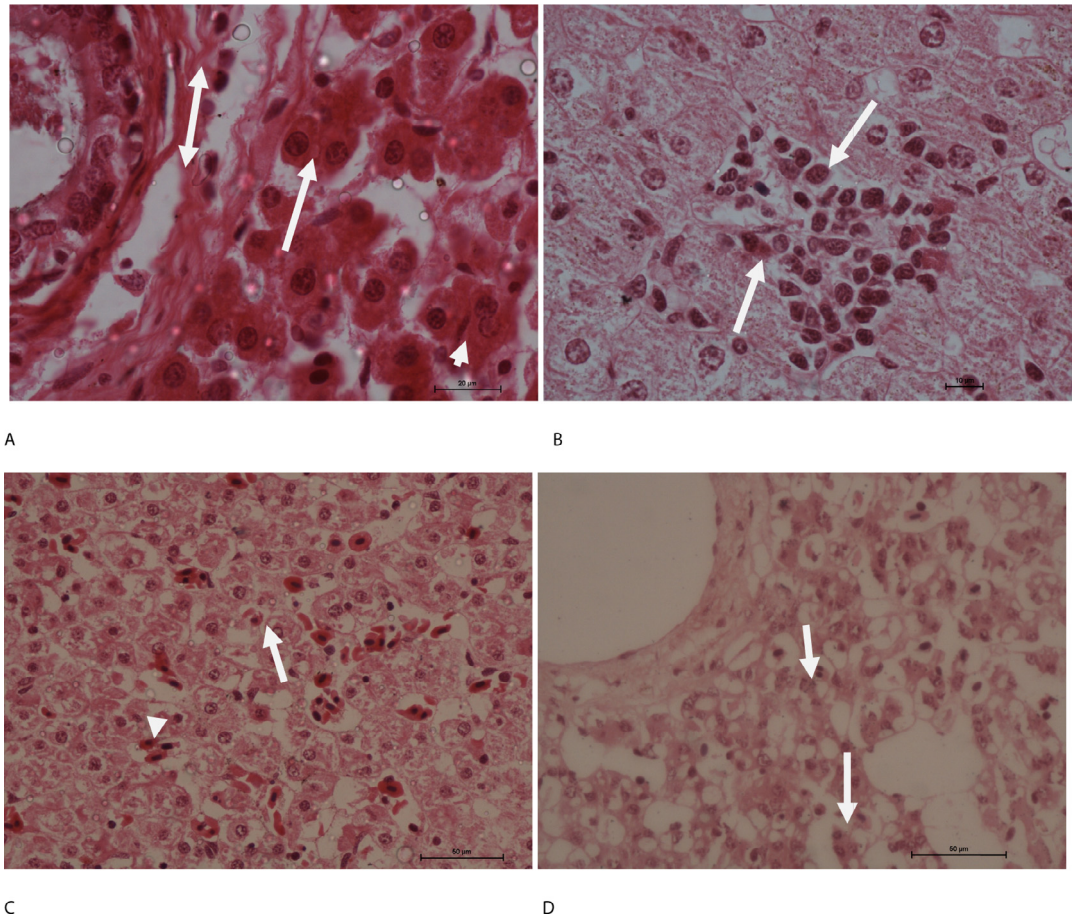

Fig. 8. A-B: Liver histomicrograph of *P. aethiopicus* from highly polluted areas (urban) at Jinja showing severe cellular alteration leading to irreparable damages. A = mononuclear infiltrations (cholangitis) in portal triad area around billiary duct (double headed arrow), binucleate hepatocytes (arrow), Küpffer cells (arrow head) showing evidence of hepatocellular pleomorphism (formalin, H&E, 40X, bars = 20 μm). B = hepatic cellular necrosis with focal mononuclear inflammatory cells infiltration (arrow) (formalin, H&E, 40X, bars = 100 μm). C-D: Liver histomicrograph of *P. aethiopicus* from less polluted areas (rural area) at Kasensero showing moderate alterations that does not impair the normal tissue functions. C = mild vacuolations (arrow head), hepatocytes nuclei displaced to the periphery either due to altered lipid metabolism or mitochondrial effect (glycogen storage) (arrow) (formalin, H&E, 20X, bars = 50 μm). D = cellular degeneration and irregular hepatocytes due to excessive glycogen accumulation, inflammatory and pyknosis cells are evident (arrow) (formalin, H&E, 10X, bars = 50 μm).

Table 4
Prevalence of some abnormalities observed in the liver of fish species from less and highly polluted areas of Lake Victoria, Uganda (outside the bracket = number of fish observed with that liver abnormality, in bracket = percentage of fish observed with that liver abnormality, - = cases were not found).

Liver abnormality	% species in less polluted areas (Rural)			% species in highly polluted areas (Urban)			Total
	O. niloticus	*L. niloticus*	*P. aethiopicus*	*O. niloticus*	*L. niloticus*	*P. aethiopicus*	
Normal liver	10(83.3)	12(75.0)	3(50.0)	2(16.7)	4(25.0)	3(50.0)	
Vacuolation	26(28.9)	10(26.3)	1(5.9)	64(71.1)	28(73.7)	16(94.1)	
Pyknotic cells	15(25.4)	3(21.4)	3(25.0)	44(74.6)	11(78.6)	9(75.0)	
Macrophage aggregate	8(22.9)	2(12.5)	2(33.3)	27(77.1)	14(87.5)	4(66.7)	
Küpffer cells proliferation	2(28.6)	–	1(50.0)	5(71.4)	2(100.0)	1(50.0)	
Leucocytes infiltrations	7(31.8)	4(23.5)	3(75.0)	15(68.2)	13(76.5)	1(25.0)	
Hepatopancreas increase	8(19.5)	9(39.1)	–	33(80.5)	14(60.9)	–	
Foci of cellular alterations	4(21.1)	3(23.1)	4(44.4)	15(78.9)	10(76.9)	5(55.6)	
Irregular hepatocytes	10(35.7)	4(36.4)	1(14.3)	18(64.3)	7(63.6)	6(85.7)	

semi-quantitative indices for interpretation and assessment (Lukin et al., 2011; Paulo et al., 2012; Dane and Sisman, 2017). Semi-quantitative liver tissue evaluation of *O. niloticus*, *L. niloticus*, and *P. aethiopicus* revealed moderate to severe alterations with significant differences among species, sites and sexes. The mean liver DTA scores for *O. niloticus* (less polluted areas = 33 ± 38, more polluted areas = 76 ± 93), *L. niloticus* (less polluted areas = 29 ± 47, more polluted areas = 48 ± 60); however *P. aethiopicus* (less polluted areas = 145 ± 99, more polluted areas = 78 ± 148) did not show this effect. The former two species clearly showed discernible defects in more polluted than less polluted sites. These suggest deleterious effects of industrial and agrochemical contaminants on fish from both more polluted and less polluted areas. Despite the restriction on certain chemicals by the Uganda Agricultural Chemicals Control Act, 2006, use of agrochemicals including DDT, endosulfan, lindane, dieldrin, dithane and antracol in the Lake Victoria catchment is ongoing. Out of 366 samples examined for liver lesions, 80.1% were affected by varying degree of tissue alterations,

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i.e. slight alteration (8.2%), moderate alteration (41.5%), severe lesion (18.6%), and irreparable damage (11.8%). Lang et al. (2006) reported a similar prevalence (83.0%) of liver alteration in 436 female flounders (*Platichthys flesus*) from the Baltic Sea, categorized as non-specific, early toxicopathic, pre-neoplastic and neoplastic lesions. Further, up to 90% prevalence of hepatocyte nuclear alterations in the liver of sharptooth catfish (*Clarias gariepinus*) from Gauteng dam, South Africa was recorded (Marchand et al., 2009). We found the incidences of normal liver (without irregularities) were higher in less polluted compared to more polluted areas. The level of effect of contamination in the liver depends on the duration of the exposure and mode of toxic actions of the contaminant. Notably, fish liver DTA scores in inshore and offshore regions were not different in our study. Nonetheless, the scores were higher in the dry seasons, consistent with the assertion that runoff deliver chemical contaminants to the aquatic environment in wet seasons that settle to the bottom with their effects on fish delayed until the dry seasons (House et al., 1993).

Hepatopancreas in fish

Hepatopancreas is exocrine pancreatic tissue in the liver of many teleost fishes, consisting of a large number of acini. Nejedli and Gajger (2013) described hepatopancreas in fish liver as islets of dispersed exocrine pancreatic tissue. Further, Mekkawy et al. (2012) described acinus in hepatopancreas, as conical glandular cells with deeply stained nuclei, eosinophilic cytoplasm and basophilic nuclei. Miura et al. (2013) categorized fish liver into two basic types; those that contain pancreatic tissue (hepatopancreas) and those that do not. The liver of *O. niloticus* 8 (19.5%) and *L. niloticus* 9 (39.1%) from less polluted areas had lower proliferation of hepatopancreas compared to those of *O. niloticus* 33 (80.5%) and *L. niloticus* 14 (60.9%) from more polluted areas. Therefore, prevalence of hepatopancreas in highly polluted sites 17 (26.6%) was comparably lower than 47 (73.4%) recorded in species inhabiting less polluted areas of the lake. Further, higher proliferation and dilation of hepatopancreatic tissue in *O. niloticus* compared to *L. niloticus* was observed. However, hepatopancreas was not observed in the liver of *P. aethiopicus*, probably due to its differential feeding habit or adaptation to environmental changes. To explore presence of hepatopancreas in liver of fish from Adriatic Sea (Croatia), common pandora fish (*Pagellus erythinus*) showed a larger proportion of hepatopancreatic tissue (14.9%), while whiting fish (*Merlangius merlangus*) showed a smaller proportion of 4.9% (Nejedli and Gajger, 2013). Similar to our findings, hepatopancreas was found in the liver of 21 fish species in Andriatic Sea (Croatia), but not always in the 29 species examined (Nejedli and Gajger, 2013). Nejedli and Gajger (2013) reported that pancreatic exocrine tissue in some species develop around the portal vein during ontogenesis and remain permanently as extra hepatic tissue. Nonetheless, absence of hepatopancreas in liver parenchyma depend on feeding habit of the species, or adaptation to non-specific stress response in aquatic environment (Segner and Storch, 1985). Indeed, hepatopancreas alteration in liver relate to chemical contamination in the aquatic environment, and is focused on the medullar region, i.e. medial and proximal zones (Sousa and Petriella, 2007).

Macrophage aggregates

These are liver cells that appear as dark pigmented substances, due to high accumulation of melanin, hemosiderin and lipofuscin (Steinel et al., 2017). Such cellular aggregates represent potential response to physiological stress or cell damage (Wolf and Wheeler, 2018). The present study showed higher percentage (78.9%) of macrophage aggregates in liver cells of *O. niloticus*, *L. niloticus* and *P. aethiopicus* from more polluted sites compared to 21.1% in less polluted sites (Table 4). Therefore, increasing pollution level of the lake from urban runoff may induce the accumulation of toxic substance in the liver. In fish, melanomacrophage centers in hepatocytes increase in size with environmental stress, hence, such pathological conditions are accepted as biomarkers for assessing chemical pollution in the environment (Hartley et al., 1996; Barst et al., 2015). A study on heavy metal contamination and hepatic toxicological responses in brown trout (*Salmo trutta*) revealed hepatic disturbances related to melanomacrophage centers (Jaffal et al., 2015).

Vacuolation in the liver

Fish liver vacuolation (lipidosis, steatosis or fatty degeneration) refer to partial or complete clearing of hepatocyte intracellular fluids or cytoplasmic matrices in stained histologic sections as toxicological responses (Wolf and Wheeler, 2018). Usually, hepatocyte vacuolation cause organelles certain distensions, a condition that occurs under glycogen shortage or stored energy in the liver in the form of lipid and glycogen (Wolf and Wheeler, 2018). Although vacuoles have been observed in normal liver of captive fish, fewer numbers are situated near the nuclei or scattered in the hepatocytes. Prevalence of vacuolation was higher in species collected from highly polluted areas of the lake (74.5%) compared to those in less polluted areas (25.5%). Further, vacuolation in the liver was more severe in males than in females; and generally, vacuoles appeared as clear circular spaces that pushed nuclei to the periphery. Thus, it appears as though the increasing environmental stress is adversely affecting the fish health in Lake Victoria. Trowell (1946) and Wagenaar and Barnhoorn (2018) reported that vacuolation is often formed during liver development in severe anoxic conditions, or in necropsy materials. The condition alters intrasinusoidal blood pressure and creates hydropic infiltrations in liver cells. Anoxic vacuolation is associated with increased liver mass and significantly reduces the HSI of fish (Sykes et al., 1976). Kranz and Peters (1985) reported a degree of fat storage in hepatocytes, which differ according to type and amount of food consumed, fish species, sex and reproductive season. Hepatic lipidosis is a risk factor due to excess intake of high-fat foods and failure of spawning conditions in female egg-layers, where much fat in the egg yolk are reabsorbed and redistributed to the liver (Speare, 2000).

Cellular hypertrophy

Abnormal cell growth was observed in livers of fishes examined. The incidence rate of irregular hepatocytes (67.4%) in the livers from highly polluted sites was pathologically severe. Taddese et al. (2014) reported that diffuse chemical contaminants in the liver reach gastrointestinal tract via hepatic portal vein and congest microcirculation in hepatic parenchyma, leading to cellular hypertrophy. However, certain swellings in the hepatocytes block sinusoids and perisinusoidal spaces (space of Disse) and cause lipid degeneration, which further congest and lower hepatocyte metabolizing capability. Küpffer cells of the liver, which utilize globin and iron from haemoglobin, were observed with prevalence of 72.7% of fishes from highly polluted sites of Lake Victoria. Further, Kupper cells proliferation in *O. niloticus* (71.4%), *L. niloticus* (100%) and *P. aethiopicus* (50%) were observed from highly polluted sites. The cells produce bilirubin which is conjugated into glucuronic acid and sent to the bile. Bilzer et al. (2006) described Küpffer cells as the predominant cellular macrophages in the liver, lining the wall of the sinusoids. *P. aethiopicus* from Port Bell (Fig. 6b) showed proliferated Küpffer liver cells, indicating chemical environmental contamination. The accumulation of chemical contaminants in

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more polluted areas of the lake induces permanent alterations in the liver.

Macrophages play a role in alerting the immune system to the presence of invaders and maintaining homeostasis during infection (Verma and Saraf, 2017). Also, gut-derived bacteria release certain natural products for hepatoprotection (Meng et al., 2018). Consistent exposure to nutrient-derived bacteria, endotoxins and cellular debris activate macrophages to enhance release of nitric oxides and cytokines for phenotype regulation (Wink et al., 2011; Causey et al., 2018). The number of macrophages increase during chronic liver injury and cellular hypertrophy (Pellicoro et al., 2014). Distribution of macrophages is normally throughout the liver hepatocytes with higher population density at the periportal region of acini, depending on the incoming pathogens through the hepatic portal vein (Bilzer et al., 2006). However, larger Küpffer cells (macrophages) are associated with the highest production of tumor necrosis in the liver (Bilzer et al., 2006). Therefore, we observed proliferation of Küpffer cells in the liver of fish examined, suggesting inflow of toxins and pathogenic bacteria in Lake Victoria. The bio-accumulation of toxins in fish in polluted areas of the lake is a potential health risk to human consumers.

Multifocal hepatic necrosis

Cellular necrosis is associated with risk factors in the aquatic environment, including contamination from heavy metals, mycotoxins and phytotoxins, depletion of oxygen and bacterial damage of gill tissue (Speare, 2000). We observed foci of cellular alterations in liver of fish from more polluted sites with higher prevalence rates, 73.2% compared to 26.8% from less polluted sites. Alterations observed included aggregates of distinct cells within parenchyma, i.e. eosinophilic, basophilic, vacuolated or clear zones of lesions. Foci of cellular alterations were reported elsewhere in black scabbardfish (*Aphanopus carbo*) and orange roughy fish (*Hoplosthetus atlanticus*) as evidence of pathology associated with exposure to the algal toxins in the Atlantic Ocean, a north-eastern region of the Bay of Biscay (Feist et al., 2015). Several discrete areas of focal necrosis lesions were detected in the liver of two potential sentinel fish species in Kuwait's Marine environment (Al-Zaidan et al., 2015). Further, multifocal alteration of vesicular fatty change observed in *Oreochromis mossambicus* from contaminated sites along Bhima River was a strong signal associated with heavy metal contamination (Kumar et al., 2017). We found that multifocal hepatic necrosis lesions were common in liver of fish from less polluted sites, as well as highly polluted, suggesting histopathological effects of natural toxins, i.e. phytoestrogens and mycoestrogens, as well as synthetic chemicals in Lake Victoria.

Conclusion

The presence and concentrations of chemicals in Lake Victoria, Uganda induced impairment in the liver of *O. niloticus*, *L. niloticus*, and *P. aethiopicus*. Biometric (HSI and K), serological (VTG in the blood serum) biomarkers and histopathology (liver lesions) were successfully used to assess effects of pollution on fishes in Lake Victoria. Qualitative and semi-quantitative liver lesions in fishes reflected pollution in the lake. Fishes collected in more polluted areas of the lake showed poor K, abnormally high levels VTG and severe liver lesions. There is a serious implication of increasing pollution levels on commercially important fishes of the lake. We confirmed that pollution adversely affected the selected fish biomarkers. This is the first study of its kind in Uganda and indicates the potential threat to public health due to the presence of high levels of VTG and liver histopathological lesions. Besides the results having implications on the health of fishes, they also overtime may have negative impacts on the consumers of fish from the lake. This would mainly due to chemical environmental contamination, which eventually ends up in the food web within the lake. Therefore, public health, industry, and environmental protection agencies should draw lessons from this study, and take action to mitigate the risks to consumers. Considering the importance of *O. niloticus*, *L. niloticus* and *P. aethiopicus* to Lake Victoria fisheries, their use in monitoring environmental health of the lake is recommended and where necessary humans should be cautious of consuming fishes from highly polluted areas.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jglr.2019.09.024.

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