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Full Length Research Paper

Analysis of the incidence of the deficit of sanitation on the health of the populations in a context of urban growth: Case of the municipalities Yopougon, Abobo and Treichville' (Abidjan, Ivory Coast)

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The emergence of pathologies and their impacts on the health of the populations were studied in the municipalities of Yopougon, Abobo, and Treichville. This study highlights the conditions of noxious life and the health of the populations. To achieve this, a transverse investigation with the households was conducted on 300 households in 2013. It is concerned with the sources of water supply. It was noticed that 80% of the households from the municipality of Abobo, 90% from Yopougon, and 85% from Treichville use the water from public adduction network. Besides, in these municipalities, the mode of management of waste water is to eliminate the waste through autonomous works, collective works or nature. So in these municipalities, a retrospective study was made on these sanitary data registered in health centers during these years. So, in the municipality of Yopougon, the data of year 2006 produced 124446 cases of malaria, acute respiratory infections and diarrheic diseases. To Treichville, 28547 cases of morbidity were collected during the year 2008. For Abobo, the sanitary data of the year 2008 showed 89280 cases of morbidity. The children of less than 5 years of these municipalities are exposed to a lot of diarrheic diseases; with 56.58% cases in Yopougon, 40.47% in Treichville and 42.03% in Abobo.

Key words: Health of the populations, diarrhea, malaria, acute respiratory infection.

INTRODUCTION

Most of the big cities in African countries are overcrowded because of the urban attraction. However, this urban growth is not supported by infrastructures or development yet. This established fact is the problem of sanitation,

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which can put the health of the populaces in danger. Indeed, the degradation of the environment is the main factor that affects health, with a direct and negative incidence on human well-being (Sy, 2014). According to the World Health Organization, the environmental factors are responsible for more than 21% of the global load of diseases (WHO, 2010). In these African cities, household wastes litter the streets. Besides, the bad conception of sanitation work entails foul smells, which is the origin of the acute respiratory infections (Yapo et al., 2013). The city of Abidjan is not left out in this type of development. It is a metropolis of almost 3.6 million inhabitants, with an annual average growth rate of 3.2%. This city represents 43.8% of the urban population of Ivory Coast (United Nations, 2006). This strong growth of the population in Abidjan ended in the production of diverse waste household as industrialists. In this city, waste water is directly rejected in the receiving environment without any treatment. So the water supplied to the populations is of doubtful quality because of the bad conditions of distribution. Indeed, this water is very often contaminated because of the intrusion of waste water in the drinkable water distribution system (Yapo et al., 2013). This increases the risks of development of the diarrheic diseases (Koné et al., 2014). The diarrheic diseases established the second cause of morbidity for those less than 5-year-old children in Africa, in the South of Sahara and more particularly in Ivory Coast (Koné et al., 2014). In addition to this, the bad drainage of waste and pluvial water generates a development of larvae breeding grounds at the origin of the pathologies for malaria (Matubi et al., 2015). According to the report of the National Program of Fight against Malaria (NPFM) in Ivory Coast in 2003, malaria is passed on all year long with an outbreak during the rainy season (Mémain, 2003). The objective of this work is to show the impact of the deficit of sanitation on the health of the populations in the municipalities of Yopougon, Abobo and Treichville. The highlighted diseases concerned are malaria, acute respiratory infections and diarrheic diseases.

MATERIALS AND METHODS

Sites of study were used to better identify the health of the populations in touch with the management of their living environment, studies were made on the sanitary data of the municipalities of Abobo, Treichville and Yopougon (Figure 1).

Presentation of the investigation's index cards

With the aim of establishing a link between living environment of the populations and their health, index cards were edited to lead investigations with the households. On these index cards, a questionnaire of investigation was developed. It was structured in six parts, which are:

(1) The identification of the household: variables such as order number allocated to the household, the names and the first names of the interlocutor;
(2) The socio sanitary equipment of the households;
(3) The water supply for drinking: The various water supplies for drinking (wells, retailers of water, public adduction in water of the Distribution Company of Water in Ivory Coast) were identified.
(4) The waste management of households: variables are relative to the practices of the populations in touch with the management of waste water, household waste and excretion;
(5) The dominant pathologies: variables concerned with the recurring pathologies, the fringes of the population, the most affected and the intentions of care in case of pathology;
(6) The individual characteristics: every member of each family is identified and characterized by its age, its sex, and its professional situation.

Information system of management (ISM)

To know the pathologies contracted by the populations of the various municipalities, sanitary data were collected by means of the ISM. The ISM contains activities of curative consultations, maternities (maternity hospitals), postnatal consultations, family planning, morbidity, sexually transmitted diseases, financial management, and management of the ISM.

Sampling of the households

Samples used in this study comprise populations living under the same roof and sharing the same needs. In these households, we had an average of 5 inhabitants. The interlocutors met in parts where there were most women. During the year 2013, inquiries were realized in the municipalities of Yopougon, Abobo, and Treichville. They were allowed to estimate the problems of sanitation which left the populations sick. To do it, the investigators identify at the households random, to interview the occupants on their various nuisances. Once they finished investigation, the households were marked and the next step was consecutively carried out.

The size of the sample depends on rates to be measured and of the desired precision as expressed in the equation (World Health Organization, 1991):

$$N = PQ / (E / L)^2$$

where N: minimal size of the necessary sample; P: estimation of the prevalence rate; Q: the value of (1-P); E: statistical risk in %; L: gap reduced for the accepted statistical risk (1, 96 for the risk 5 %).

By considering malaria, which is one of the diseases caused by a deficit of sanitation, the prevalence rate (30%) at the national level is well known (NPFM, 2003). The application of the equation with an acceptable risk of 5% succeeded in:

$$N\ P\ (1\text{-}P) / (E / 1.96)^2 \text{ is } N = 0.30\ (1\text{-}0.30) / (0.05/1.96)^2$$

This application sample was carried out on 323 households. A size of 100 samples for households, using municipality, with a total of 300 households for three municipalities, were retained.

Methods of sanitary investigation with the households

In the households, index cards were used to lead investigations with the households to understand better causes of the various pathologies, contracted by the populations and their therapeutic routes. The method of reserved investigation is the administration of questionnaires in the form of interview.

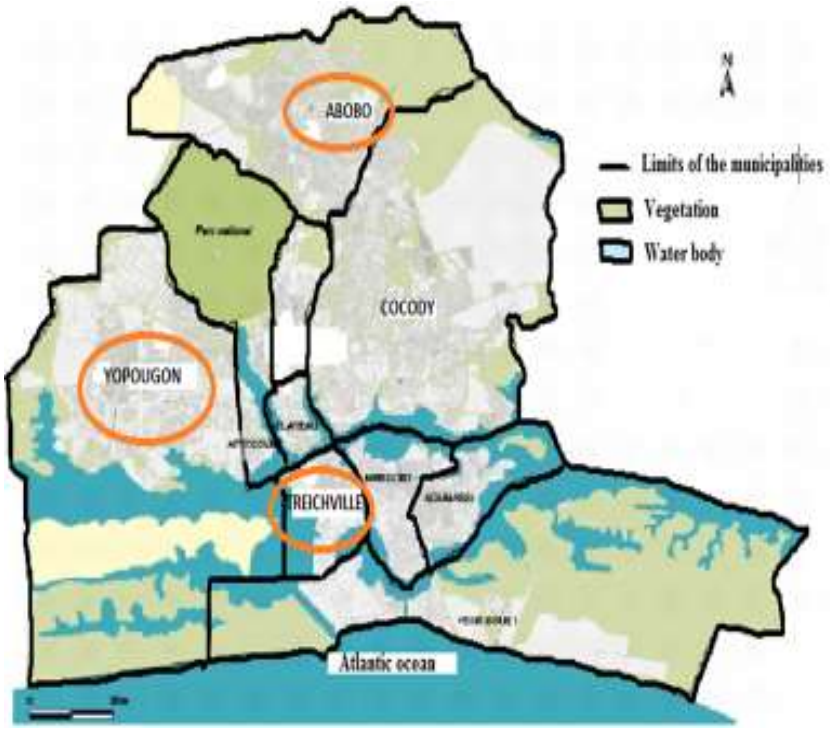

Figure 1. Map of the municipalities of Yopougon, Abobo, and Treichville.

Methods of acquisition of the sanitary data (In the sanitary structures)

To identify the pathologies contracted by the populations in these various municipalities, a retrospective study in health centers of these municipalities was made. Indeed, the structures of health monthly register the diverse activities which they lead, and these activities are recorded in the ISM. The diseases with statement compulsory are communicated every month end with the competent structures for the organization of a possible sanitary retort. In these municipalities, it was necessary to make a retrospective study on these sanitary data registered by health centers during various years. For the municipality in Yopougon, the data were of 2006. In this municipality, the sanitary structures supplied 124446 cases of morbidity for malaria, acute respiratory infections, and diarrheic diseases. In Treichville, hazard was used for the data of year 2008 with 28547 cases of morbidity. In Abobo, the data were from year 2008. In this municipality, the data was collected for a total of 89280 morbidity case.

RESULTS AND DISCUSSION

Presentation of the sanitation in the municipalities

The results of inquiries led with the households show that, 80% of the households of the municipality of Abobo use water resulting from the network of public adduction in drinking water. This result borders those of the municipality of Yopougon and Treichville; with 90 and 85% respectively. As for the use of the water of the retailers, the investigation showed that there is 7% of the households which use them in Yopougon, 15% in the municipality of Abobo and 9% in Treichville. Besides, the use of the water of wells for the consumption is very unimportant in these districts. In the municipality of Yopougon there is 3%, to Abobo 5%, and to Treichville 6%. The analysis of Figure 2 shows that the water resulting from the network of adduction is used a lot by the populations.

In the districts of Yopougon, Abobo and Treichville municipalities, excretion of human beings are evacuated in the autonomous works, the collective works or in the nature. According to the results of the investigations, approximately 53% of the households of Abobo use the autonomous works. This result is higher than that of Yopougon (25.87%). On the other hand for Treichville, these works are used much more with 88% of the households.

Figure 3 shows that for the management of waste water in the city of Abidjan, individual works are used a lot.

Therefore the investigation showed that, the percentage of the households which pour excretion in the nature is unimportant.

The evacuation of household waste in the districts of the municipalities of the city of Abidjan is made either in garbage containers, or in wild deposits. According to the results of the investigations, 29% of the households of the municipality of Yopougon use tubs, while 71% of the households pour their household waste in wild deposits.

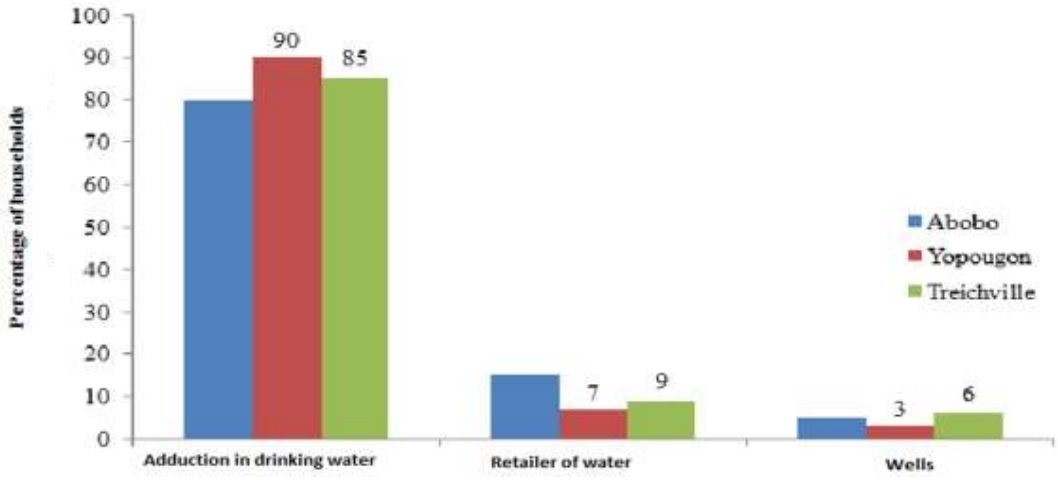

Figure 2. Water supply of drink in the households.

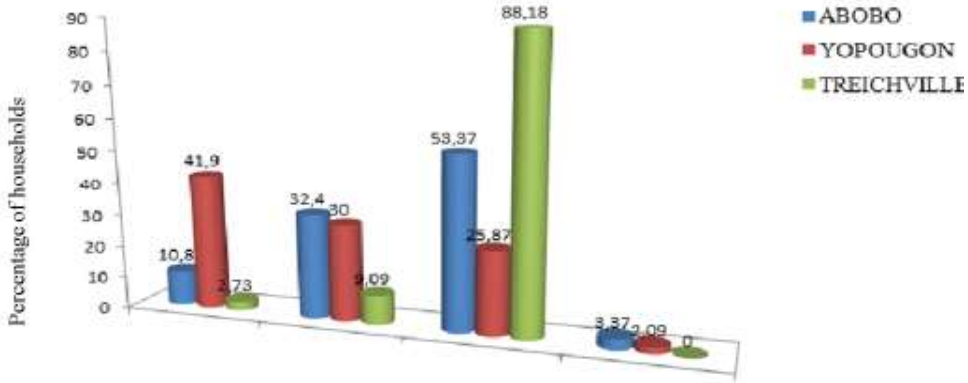

Figure 3. Proportion of use of the works of purification by the households.

In the municipality of Abobo, there are 79% of the households which use wild deposits; while 21% use garbage containers. To Treichville, there are 63% of the households that use wild deposits; while approximately 37% pour their household waste in garbage containers.

Figure 4 shows that there are many wild deposits in districts and fewer garbage containers.

Sanitary practices of the populations

Table 1 shows that in the municipality of Abobo, 73% of the households are devoted to auto medication; while 27% of the households opt for hospital care in case of disease. The same report is made in the municipalities of Yopougon and Treichville where there are respectively 68% of households for the auto medication, 22% for the medical consultation and 62% of the households which are interested in the auto medication; while 28% of the households opt for a medical consultation in case of disease.

In these municipalities, the populations are devoted to the auto medication very often for their medical care.

Evolution of the morbidity in the municipalities

Figure 5 shows that the number of people having contracted the malaria in the municipalities of Yopougon, Abobo and Treichville increases from January till July and decreases from July till December, respectively in 2006, 2005, and 2008. June and July is the peak, corresponding to the period of big rainy seasons.

In the municipality of Abobo, the number of people increases the diarrhea growth, where a peak is observed from January till June. After June, a diminution of this number was observed until December. Contrary to the municipality of Abobo, in the municipality of Yopougon, a

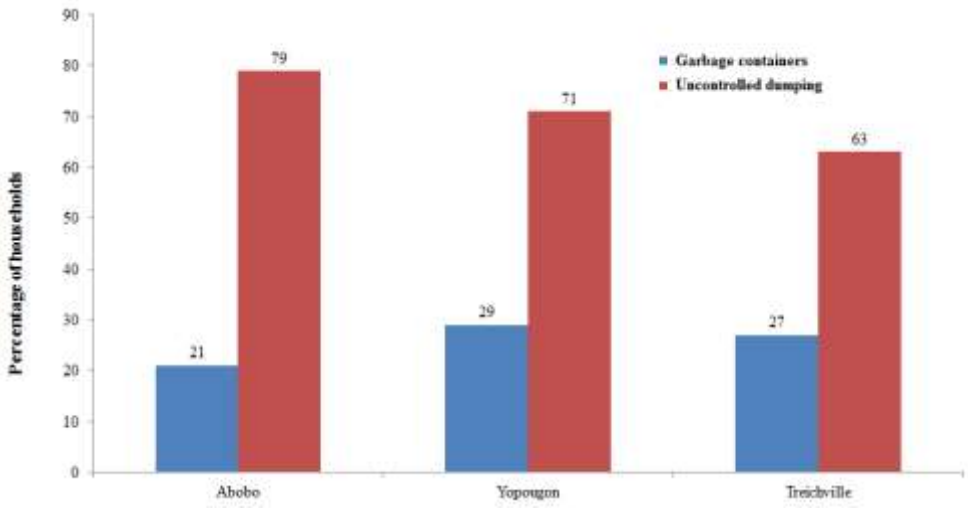

Figure 4. Proportion of households using garbage containers to evacuate their waste.

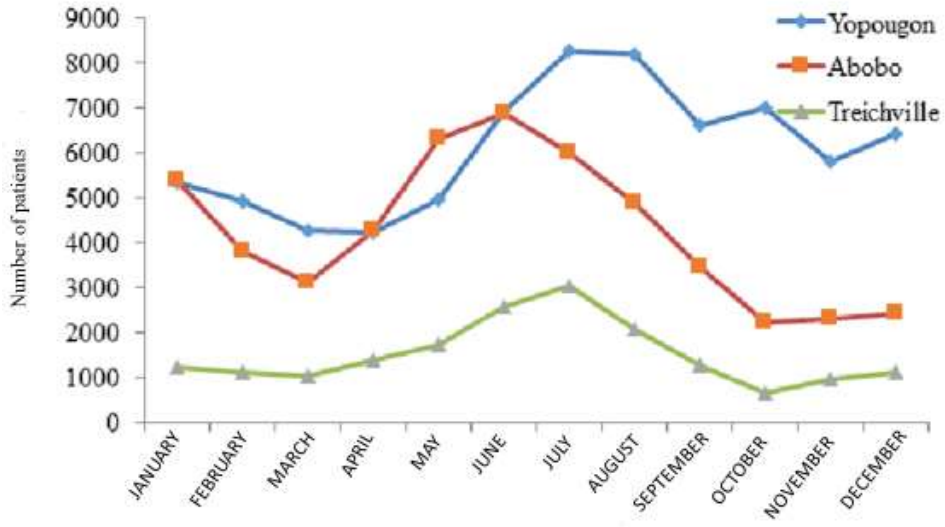

Figure 5. Evolution of the number of cases of malaria in the sanitary structures.

Table 1. Intention of care in case of pathology.

Municipalities	Intentions of care	
	Health centre (%)	Self-medication (%)
Abobo	27	73
Yopougon	22	68
Treichville	62	28

peak in August was observed. This number evolves in the municipality of Treichville, with a small peak observed in June (Figure 6).

As for the diarrhea, the evolution of the number of sick during the year differs from a municipality in another one. There were three municipalities of the present Treichville with low staff, with cases of diarrhea.

Figure 7 shows that the number of people having

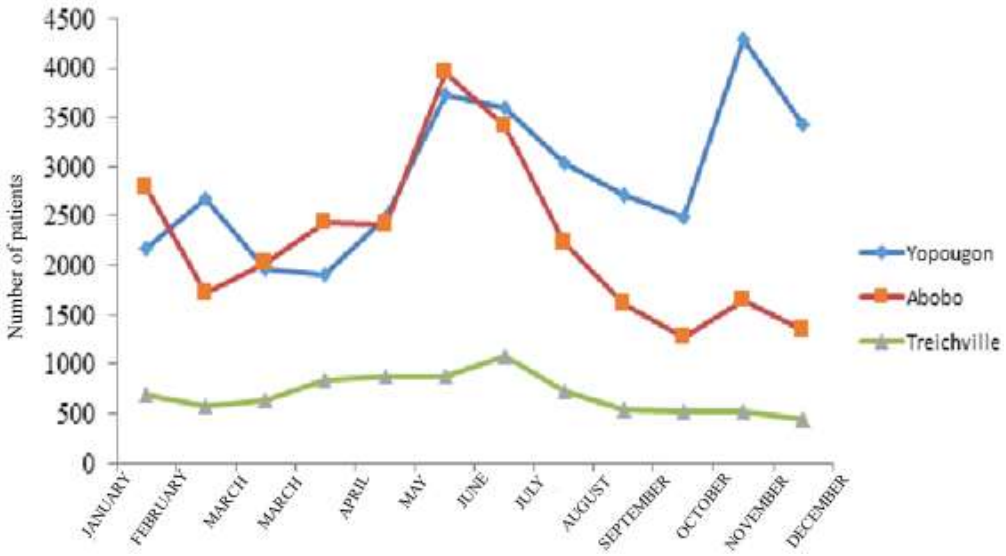

Figure 6. Evolution of the number of cases of diarrhea registered in the sanitary structures.

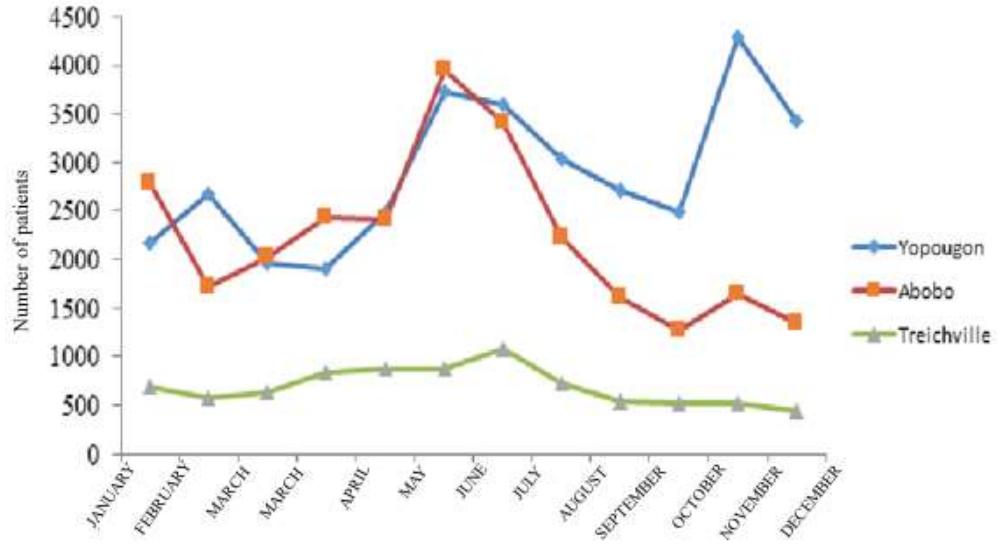

Figure 7. Evoluation of the number of cases of IRA(IRAS) in the sanitary structures.

contracted the acute respiratory infections in the municipality of Yopougon increases from January till June, reaches a peak before decreasing until October, to grow again and reach another peak in November. In the municipalities of Treichville and Abobo, the number of consultation evolves up until June, before decreasing till December.

The rate of exposure of children less than 5 years was high in 2005, 2006, and 2008, respectively in the municipalities Yopougon, Treichville and Abobo. In the municipality of Yopouon, there are 56.58% of the children less than 5 years who contracted the diarrhea during the year, as against 36.85% for the malaria and 6.57% for Acute Respiratory Infections (Table 2). So the municipalities of Treichville and Abobo presented a strong representativeness of diarrheas with respectively 40.47% proportions and 42.03%. In these municipalities, Acute Respiratory Infections occupy an important proportion which belongs to the order of 41.25% for Treichville and 35.31% for Abobo. On the other hand, malaria is less contracted by children of less than 5 years for Treichville (18.28%) and Abobo (22.66%).

So the municipalities of Treichville and Abobo present a strong representativeness of diarrheas with 40.47% proportions and 42.03% respectively. In these municipalities, Acute Respiratory Infections occupy

Table 2. Rate of exhibition of the children least than 5 years in the pathology.

Communities	Pathologies		
	Malaria (%)	Diarrhoea (%)	Acute respiratory infections (%)
Abobo (Year 2008)	22.66	42.03	35.31
Yopougon (Year 2005)	36.85	56.58	6.57
Treichville (Year 2006)	18.28	40.47	41.25

important proportions, which belong to the order of 41.25% for Treichville and 35.31% for Abobo. On the other hand, the malaria is less contracted by the children of less than 5 years to Treichville (18.28%) and to Abobo (22.66%).

DISCUSSION

This work uses an interdisciplinary approach in the study of the sanitary conditions and the sanitary risks for the public health. It reveals that the accessibility of the populations to the drinking water is very important. According to the studies of Coulibaly et al. (2004), 99% of the households of the municipality of Port-Bouët are connected to the networks of drinking water. This result borders those of the municipality of Yopougon and Treichville, where we are respectively 90 and 85%. On the other hand in Abobo, 80% of the investigated households use water resulting from the public adduction. The water of the retailers is used by 7% of the households in Yopougon, 15% in the municipality of Abobo and 9% for Treichville. Besides, the use of the well water for the consumption is very unimportant in these districts; where 3% of the investigated households are concerned to Yopougon, 5% for Abobo and 6% for Treichville. This difference could give some explanation on one hand by the efforts of setting-up of sources of drinkable waters in these municipalities and on the other hand, by raising sensitization of the population to the importance of the use of a good quality of water for human consumption (Coulibaly et al., 2004). This study also showed that households generally use the autonomous works of purification. In these various municipalities, the results showed that more than 50% of the investigated households use this system of purge for waste water. The use of these autonomous works of purification was postponed in the works realized by Yapo et al. (2013) in the municipality of Yopougon. So, Kuitcha et al. (2008) found in Cameroon that the autonomous works of purification are used a lot by the households. However, the bad conception of these works and their overexploitation contributed to the deterioration of the health of the populations (Dongo et al., 2008). Indeed, the diarrheic diseases are caused by several parasites including the Salmonellas that are seen in unhealthy environments, due to a defective hygiene (Koné et al., 2014). Besides, according to the World Health Organization (2001), studies carried out on the diarrheic diseases showed that they make 1.5 million deaths in developing countries. Much more, there was 21% of infant mortality in developing countries (UN-WATER, 2006). The investigations led in health centers gave an infantile morbidity of 46% because of the diarrheic diseases. This result is found in the works realized by Yapo et al. (2013) who showed that, the poor circles of developing countries are the most affected by the diarrheic diseases; especially the fringe of the children of less than 5 years.

Besides, the proportion relative to the malaria registered in health centers is higher than that found in the municipality of Yopougon by Dagnan et al. (2002) which is 23.3%. This proportion borders found in the studies was realized in the municipality of Port-Bouët (46%) by Coulibaly et al. (2004). This could be explained by the stagnation of waste water due to the expulsion of these on public highways. This report was made by Dongo et al. (2008), that among the districts of the municipality of Yopougon, that of Doukouré is the most affected by the problems relative to the purification. Besides, the results obtained as for the malaria are similar to those recorded in developing countries where malaria is endemic (WHO, 2001). Also, the report on the state of progress of the National Program of Fight against Malaria in Ivory Coast (2003) indicates that, malaria is passed on all year long with an outbreak during the rainy season. This report was made in a study by Yapo et al. (2013) showing that, malaria is contracted a lot during the rainy seasons.

Concerning the acute respiratory infections, the study shows that peaks are observed in February, July, and November. Peaks observed simultaneously in February, during dry season; whereas the July corresponds with the big rainy seasons. These observations were also told by Guedonon (1987) noticed in Benin that acute respiratory infections are much more pronounced during the hot and wet seasons. Besides, the results show that the acute respiratory infections of less than 5-year-old children are around 27%. This proportion is widely below 88% found in the works of Bakonde et al. (1998) realized in Togo. These results show that the Ivory Coast sanitary policy in favor of the children of this age bracket turns out to be effective, because the acute respiratory infections are the cause of 4.3 million deaths a year less than 5-year-old

children; which represents 21.3% of all the deaths of this age group (WHO, 1991).

As for the recourse to the medical care, inquiries with the households showed that more than 60% of the households of the various municipalities devotes to the auto medication. Studies carried out by Bossart (2002) in Benin shows the important role of the auto medication in the treatment of the pathologies. Indeed, the therapeutic virtues of certain healing plants used by the populations in the treatment of malaria (Cassia occidentalis) are scientifically proved (Tona et al., 2004). So, it is necessary to note that the guava is sometimes used for the treatment of the pains gastroenteritis-intestinal and cases of diarrhea. Clinical trials show the efficiency of some substances extracted from guava in the treatment of diarrheas (Lozoya et al., 2002).

Besides, other studies on 200 Indian mothers, whose children suffered from respiratory infections showed that, 25% of the mothers used some honey to handle the cough of their children, while 27% use ginger (Tona et al., 2004). But for Kouadio et al. (2006), a treatment without medical consultation can be more expensive than the treatment after the diagnosis of a modern specialist. So, the ignorance of the households on the choice of an appropriate therapeutic route countered as an economic risk factor for the household in front of pathologies. To do it, a raising sensitization of the populations to a good hygiene by the authorities is necessary, to protect and improve the health of the populations. Thus, it is necessary to recommend the use mosquito nets populations, to protect them from mosquito bites. Besides, the authorities have to improve the quality of the water consumed by the populations. Gutters have to be cleaned and septic tanks should be drained away regularly when they are full.

Conclusion

Diarrheic diseases, malaria and acute respiratory infections constitute a real problem of public health to Yopougon, Abobo and Treichville. Malaria and respiratory infections are contracted a lot by the populations during the rainy season contrary to the diarrheic diseases which are caused by a defective hygiene of the environment and the bad practices of the populations regarding purification. Among the various pathologies, diarrheic diseases are contracted a lot by children of less than 5 years. To mitigate this problem, one solution of the viable solutions of effective fight against these pathologies is the eco systematic approach in the human health. The results of the study will be useful particularly for the authorities of these various municipalities who manage the problems of sanitation. They will contribute to the design of a new politics concerning the restoration of the living environment for a greater well-being of the populations.

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CONFLICT OF INTEREST

The authors have not declared any conflict of interest.

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Maternal and foetal toxicity induced by exposure to mixture of dimethoate and cypermethrin in albino rats

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The use of pesticide mixture to combat increased resistance by pest, to single chemical insecticide has brought about an increase in the use of pesticide mixture from different class, with its attendant toxicity. The objective of this study was to evaluate the maternal and foetal toxicity associated with dimethoate and cypermethrin, the two insecticides that are normally mixed to reduce pest resistance. 100 confirmed-mated (gravid) females were assigned at random among the four groups (control – tap water only): group 1- very low dose-10 mg/kg/day of Cypermethrin (5.3% LD_{50}) + 1.0 mg/kg/day Dimethoate (0.7% of LD_{50}); group 2- intermediate dose- 19 mg/kg/day of Cypermethrin (10% LD_{50}) + 1.4 mg/kg/day Dimethoate (0.9% of LD_{50}); and group 3- high dose- 38 mg/kg/day of Cypermethrin (20% LD_{50}) + 12.8 mg/kg/day Dimethoate (8.5% of LD_{50}). The regimens were administered orally at gestation days (GD) 6-20 to pregnant rats. The dams were examined for mortality, moribundity, pertinent behavioural changes and signs of overt toxicity. Animals were weighed on day 0, and once at every 3-day intervals during the dosing period and on GD 21. The pregnant rats were sacrificed by decapitation on GD 21, the uteri were removed and the fetuses examined for litter weight, size, resorption, sex ratio, absolute and relative organ weight. The results showed that combined pesticide exposure caused overt toxic signs in the dams. However, the maternal body weight and relative organ weight were not adversely affected except in the heart that showed significant alteration. Although, the litter weight was not adversely compromised, the result showed that the prenatal exposure to pesticide mixture caused increased foetal resorption, decreased the litter size and offsprings' male/female ratio. The study concludes that prenatal co-exposure to cypermethrin and dimethoate has adverse consequences on some maternal and foetal parameters in albino rats.

Key words: Pesticide mixture, litter size, sex ratio, litter weight, maternal relative organ weight.

INTRODUCTION

Pesticides are widely used in food production systems and public health in many countries because of the need to feed the ever-increasing human population and protect them from vector-borne diseases (Bhaskar et al., 2014; Gabr et al., 2015). Pesticide applications have increased dramatically since the 1960s (Olgan et al., 2004). The

wide use of pesticides has made them quite ubiquitous. The reality is that human exposure and the related health effects in humans as well as in wild/domestic animals have become a serious concern (Crumpton, 2001).

Human exposure to pesticides is rarely limited to a single chemical. People are exposed daily to a variety of chemicals in foods, drinks, cosmetics and indoor and outdoor pollutants (Marinovich et al., 1996). Agrochemicals are often applied in combinations and it is not uncommon for many classes of pesticides, such as insecticides, herbicides and fungicides, to be used on the same crop (National Agricultural Statistics Service, 2005). Furthermore, the increase incidence of pest resistance to specific pesticide has led to formulations containing two or more pesticides. Each active ingredient in the formulation has a specific mode of action for controlling a pest, and each active ingredient has its own possible side effects on non-target animals and humans exposed to it (Colborn, 2006). In fact, mixed exposures are the rule rather than the exception indicating that exposure assessment, hazard identification, risk assessment and risk characterization should focus on mixtures rather than single chemicals (Liu et al., 2006). Attempts at predicting the toxicology of mixtures based upon the knowledge of individual chemicals often leads to the wrong conclusions (Marinovich et al., 1996). The effect of the interaction between pesticides in combination is not always predictable, as such combinations may result in synergism, additive effects, potentiation or inhibition. Two or more compounds may show additive, antagonistic, or synergistic interaction or each may act on totally different systems and thus not interact (Liu et al., 2006). Synergism of pyrethroids by organophosphorous insecticides has been demonstrated. For instance, Martin et al. (2003) showed significant synergism for mixtures of cypermethrin/ethion; deltamethrin/triazophos and deltamethrin/chlorpyrifos. There is a potential hazard in mixed intoxication by pyrethroids and organophosphorous insecticides, due to the fact that the low toxicity of the pyrethroids on mammals is chiefly due to quick cleavage of molecules by esterases, which can be thwarted by esterase inhibitions (Audegond et al., 1988).

Insecticides are considered as potent pollutants of the environment that have been involved in birth defects and reproductive failure. Due to its widespread use and the rising instability of the foetus and the pregnant mother to toxic exposures, the adverse health effects correlated with exposure to insecticides during pregnancy have become a considerable public health interest (Stillerman et al., 2008). Mothers involved in agricultural activities before conception or during the first trimester of pregnancy have been shown to have an increased risk of having offspring with defect of the nervous system, oral cleft or multiple anomalies (Gary and Ostby, 1998). Garcia et al. (1999) have reported that fathers who were involved in agriculture had an increased risk of having offsprings with defects of the nervous or musculoskeletal systems. Professional applicators of pesticides have been reported to show specific congenital anomalies in their offsprings (Shaw et al., 1999). Chronic exposure to organophosphorous and other pesticides during preconception and perinatal periods can induce a range of adverse birth outcomes (Gomes et al., 2008). In animal models, chronic maternal and paternal exposure to organophosphorous pesticides during the preconception period and early pregnancy can increase the risk of congenital anomalies in offsprings.

Organophosphorous pesticides are reported to induce a variety of symptoms leading to cholinergic morbidity among farm workers and pesticide handlers (Gomes et al., 1999a). These pesticides are also reported to inhibit cholinesterase activity, affect neurological and cognitive function among other health effects in humans and non-target mammalian species (Gomes et al., 1999; Sinha and Shukla, 2003; Young et al., 2006). Some of the organophosphorous pesticides are mutagenic and alter cell division; others are oestrogenic and alter reproductive and central nervous system function (Gomes et al., 2008).

Dimethoate (DM) [(0, 0-dimethyl-S (N-methylcarbonyl methyl) phosphorodithioate)] is an organophosphate insecticide with numerous uses on field, agricultural crops and ornamentals (Gallo and Lawryk, 1991). Its persistence in crops and soils may further enhance its propensity of adverse health consequences in man and other non-target species (IPCS/WHO, 1992). The residue of DM and its analog (omethoate) were found in many food stuffs including cow milk (Srivastava and Raizada, 1996). Although, DM remains one of the most widely used pesticides in the world, there is limited information regarding the developmental toxicity of this pesticide (Farag et al., 2006).

In mammals, the primary site of action of organophosphate pesticides is the central and peripheral nervous systems and is by inhibiting acetylcholinesterase, a biochemical event that results in accumulation of endogenous acetylcholine at the nerve endings (Sarkar and Maitra, 1990; Gore, 2001). Several physiological and behavioral dysfunctions occur in animals after exposure to light doses of organophosphate pesticide (Ambali and Ayo, 2011). Therefore, there is the possibility that DM can affect humans and animals in their natural habitat. DM has been reported to cause developmental toxicity such as decreased number of implantations and live fetuses, incidences of resorptions and decreased foetal body weights (Farag et al., 2006).

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Table 1. Grouping and dosing schedule.

Group	Animal assignment		
	Cypermethrin (mg/kg/day)	Dimethoate (mg/kg/day)	Number of animals
Control	0	0	25
Very low	10.0 (5.3%of LD_{50})	1.0 (0.7% of LD_{50})	25
Intermediate	19.0 (10% of LD_{50})	1.4 (0.1% of LD_{50})	25
High	38.0 (20% of LD_{50})	2.8 (8.5% of LD_{50})	25

Pyrethroid insecticides have achieved widespread agricultural and environmental health applications due to their strong insecticidal properties. They are one of the most frequently used classes of pesticides (Roberts and Hutson, 1999) apparently due low toxicity to mammals than the other classes of insecticides, such as organochlorines, organophosphates and carbamates (Syed et al., 2009). Because of their low acute human toxicity, pyrethroids are
widely used to control insects in and around homes (Freeman et al., 2004). The toxicity of pyrethroid insecticides to mammals received much attention in recent years because animals exposed to these insecticides showed changes in their physiological activities besides other pathological features (Glass, 2008). Certain pyrethroids exert hormonal activity that may alter early neurologic and reproductive development, and they are known also to elicit a range of immunotoxic and neurotoxic effects in humans and other mammals. Also, exposure to pyrethroids has been reported to contribute to reproductive dysfunction, developmental impairment and cancer (Garey and Wolf, 1998; Landrigan et al., 1999).

Cypermethrin is a synthetic pyrethroid insecticide widely used all over the world against a varying range of pests in agriculture, public health and animal husbandry (Al-Hamdani and Yajurvedi, 2010). It is a known neurotoxicant and primarily targets sodium channel in the nerve membrane of both central nervous system and peripheral nervous system (Cox, 1996; Narahashi, 1996; Ahmad et al., 2011; Singh et al., 2012). Since its introduction, it has become one of the mostly widely used insecticides in the developing countries (Assayed et al., 2010; Cremonese et al., 2014; Dewailly et al., 2014). Assayed et al., (2010) reported toxic effects of cypermethrin when exposed to either target or non-target organisms.

It can cross the placenta barrier, thereby affecting physiological functions associated with foetal neurological development (Dewailly et al., 2014) and foetal weight (Madu, 2015). The aim of the present study was to evaluate the effect of prenatal co-exposure to cypermethrin and dimethoate on some foetal parameters in male albino rats.

MATERIALS AND METHODS

Chemicals and preparations

Commercial grade Cypermethrin (EC; Nagarjuna Agrochemical limited, Punjagutta, Hyderabad, India) and commercial grade dimethoate: (VITOATE 40EC; Manufacturer: Asiatic Agricultural Pte Company, Singapore) were obtained from a reputable Agro-Allied Store in Abuja. They were dissolved in tap water to make appropriate concentrations used to dose the various treatment animals (US, EPA, 1989; Galo and Lawryk, 1991), while those in the control group were given tap water only (2 ml/kg).

Test animals

The experimental animals were albino rats obtained from the animal breeding facility at the Department of Pharmacology, University of Jos, Plateau State, Nigeria. The animals were kept in the animal house in the Department of Pharmacology and Toxicology of the National Institute for Pharmaceutical Research and Development (NIPRD), Idu-Abuja, Nigeria. They were housed in groups of not more than five in plastic cages with beddings of wood shavings. All animals in the study were fed rodent diet compounded using growers chick mash. Tap water was made available *ad libitum.* Animals used in this study were handled and maintained in compliance with the National Institutes of Health Guide for Care and Use of Laboratory Animals (Garber et al., 2011), while the experiment was conducted with the approval of the Institutional Ethical Committee of NIPRD.

Mating

Three non-gravid female rats were paired with one male rats of the same strain overnight for mating purpose. The following morning, vaginal swab was taken from each of the females and mating was confirmed by the presence of sperm in a vaginal swab smear under the microscope. The day evidence of mating observed was designated day 0 of gestation (GD 0).

Animal groupings and dosing schedule

One hundred (100) confirmed-mated (gravid) females were randomly assigned among the four groups (control, very low dose, intermediate dose and the no-observed-adverse-effect level (NOAEL). The animals were housed in groups of five in plastic cages with stainless steel covers and wood shavings. Every day, from GD6 – GD 20, pregnant rats were treated with the pesticide mixture by gavage once daily according to the regimen indicated in Table 1.

Doses were selected based on data from the LD_{50} of 187 and 150 mg/kg for cypermethrin (EPA, 1989) and dimethoate (WHO, 1989), respectively. Doses were selected to ensure that the highest dose should induce some developmental and/or maternal toxicity but not more than 10% maternal mortality. Intermediate dose levels should produce minimum observable toxic effects; and the lowest dose level should not produce any evidence of either maternal or foetal toxicity.

Each animal was observed at least once daily for mortality, moribundity, pertinent behavioural changes and signs of overt toxicity. Animals were weighed on day 0, and once every 3 days during the dosing period and on GD 21. Immediately after the animals were sacrificed, the uteri were removed and the pregnancy status of each of the animals was determined.

Foetal examination and sex determination

The abdominal cavity of each pregnant dam was opened, the uterus removed and weighed before it was opened, the number and position of living, dead and resorbed fetuses were determined and recorded. The stage of resorption was divided into three groups: early, intermediate and late. Uterine horns that appeared not to be gravid were stained with ammonium sulphide, in order to be able to demonstrate foetal resorption at an early stage as much as possible.

Briefly, the uterus was inserted in 10% ammonium sulphide for 5 min and then rinsed in water. Implantation sites which appeared as “black points” were thereafter counted. If the entire uterus appears black, then the test is negative, which indicates no implantation had taken place in the uterus. The fetuses were removed and the sex and body weight of each of them were determined. The fetuses were weighed according to their uterine position (top right = 1st foetus; top left = last foetus), numbered according to Standard Operating Procedure (SOP) 6 of the Teratology Laboratory at the Department of Toxicology, Institute for Clinical Pharmacology and Toxicology, Charitè University Medical School, Berlin. Before the fetuses were carefully opened by abdominal incision, their sex was determined by judging the anogenital distance (female = smaller, male = greater distance). After opening the abdomen, locating the testes or ovaries, helped to confirm the sex of the foetus. The sex ratio for each group was then calculated.

Statistical analysis

Data expressed as mean ± SD was subjected to one-way ANOVA followed by Dunnett test. Statistical analysis was done using SPSS for Windows version 16.0 and the level of statistical significance was set at $p<0.05$.

RESULTS

Maternal clinical signs

No evidence of toxicity was seen in any of the dams exposed to a combination of 10 mg/kg body weight of cypermethrin + 1 mg/kg body weight of dimethoate. No mortality was recorded in the group and no significant behavioural changes were observed. Generally, no signs of overt toxicity were recorded at cage side observation. Similarly, no mortality was recorded in the second treatment group exposed to a combination of 19 mg/kg of cypermethrin + 1.4 mg/kg of dimethoate. However, four animals in the group, exhibited hyperactivity, tremors, spasms and hypersalivation. Unlike animals exposed to the first two combined dose levels of the pesticides, rats exposed to a combination of cypermethrin (38 mg/kg) and dimethoate (2.8 mg/kg) showed muscarinic signs characterized by hypersalivation and nasal discharges and a preponderance of signs of nicotinic cholinergic stimulation mainly muscle fasciculation, tremors, spasms and stiff gait. Two animals exhibited hyperactivity and mild clonic convulsion before death supervened.

Effect on maternal body weight

No significant differences ($P>0.05$) were observed in the body weights’ of treated and control animals.

Effect on uterine contents

With the exception of one animal which was pregnant in only one uterine horn, no abnormality was observed in the uterine contents of animals exposed to a combination of 10 mg/kg body weight of cypermethrin + 1 mg/kg body weight of dimethoate. There was no evidence of embryonic or foetal deaths/ resorption in the uteri of animals in this group. However, in the group of animals exposed to the second combined dose level of 19 mg/kg of cypermethrin + 1.4 mg/kg of dimethoate, the uterus of one of the animals had numerous blood spots indicative of late foetal resorption. Exposure to a combination of 38 mg/kg of cypermethrin + 2.8 mg/kg of dimethoate was found to result in foetal deaths *in utero* in two animals. In one of such cases, the dead foetus was intact while on the other, foetal disintegration had already taken place.

Effect on litter size

The litter size was found to be significantly ($P<0.05$) lower when animals in the treatment groups were compared with those in the control group. The litter size was lower in the treatment groups than in the control. Those in group 2 exposed to a combination of 19 mg/kg cypermethrin + 1.4 mg/kg dimethoate, recorded the least mean litter size of 7.70. This was found to be statistically significant at $p<0.05$ (Table 2).

Effect on litter weight

No statistically significant difference ($P>0.05$) was found in the litter weight between the offspring of treated and control animals (Table 2).

Effect on sex (male/female) ratio

Although, there was no statistically significant difference

Table 2. Number of fetuses/litter, foetal weight/litter, and sex ratios of fetuses of rats treated with combinations of cypermethrin and dimethoate during pregnancy.

Parameter	Mean ± SD			
	Control	10 mg/kg cypermethrin +1.0 mg/kg dimethoate	19 mg/kg cypermethrin +1.4 mg/kg dimethoate	38 mg/kg cypermethrin +2.8 mg/kg dimethoate
Number of Foetuses/litter	8.95± 1.19	8.35 ± 0.99	7.70 ±1.30*****	8.15 ±1.22
Average foetal weight/litter(g)	2.56 ± 0.60	2.46 ± 0.51	2.43 ± 0.67	2.45± 0.72
Sex ratio (male/female)	47.3/52.5	47.1/52.6	46.4/53.6	46.8/52.1

Table 3. Relative (percent of body weight) organ weights of females treated with combination of cypermethrin and dimethoate during pregnancy (n=25/group).

Parameter	Relative organ weight ± SD			
	Control	10 mg/kg cypermethrin +1.0 mg/kg dimethoate	19 mg/kg cypermethrin +1.4 mg/kg dimethoate	38 mg/kg cypermethrin +2.8 mg/kg dimethoate
Brain (g)	0.82 ±0.30	0.78 ±0.29	0.78 ±0.32	0.78±0.30
Heart (g)	0.45 ±0.15	0.44 ±0.16	0.45 ±0.26	0.37 ±0.18*****
Kidneys (g)	0.67 ±0.28	0.62±0.29	0.67±0.14	0.68±0.25
Liver (g)	3.40 ± 0.69	3.32 ± 0.11	3.60 ± 0.15	4.43 ± 0.66
Lungs(g)	0.88 ± 0.55	0.86 ± 0.62	0.85 ± 0.56	0.76 ± 0.22
Spleen(g)	0.68 ± 0.28	0.38 ± 0.01	0.41 ± 0.03	0.38 ± 0.01
Uterus+ovaries (g)	5.95 ± 2.38	3.43 ± 1.10	1.82 ± 0.59	4.89 ± 1.40

*Significant at p<0.05 for values within the same row.

(P>0.05) in the sex ratio between the offspring of treated and control animals, that of the offspring of the former were relatively lower (Table 2).

Effect on relative maternal organ weight

No difference was observed in the absolute weights of the brain, kidneys, liver, lungs, spleen, uterus and ovaries of pregnant females in the control animals as well as those exposed to three combinations of cypermethrin and dimethoate. However, when the organ weights were expressed as a ratio of body weight (relative weight), animals in the three treatment groups had relatively smaller hearts than control animals. However, there was no statistically significant difference (P>0.05) in the relative heart weight between control and treatment groups. Only animals exposed to 38 mg/kg cypermethrin + 2.8 mg/kg dimethoate, had statistically significant (p< 0.05) difference in relative heart weight as compared to those in the control group (Table 3).

DISCUSSION

The lack of evidence of foetotoxiciy in the fetuses of dams exposed to the combination of 10 mg/kg of cypermethrin + 1 mg/kg of dimethoate and the group that received 19 mg/kg of cypermethrin and 1.4 mg/kg of dimethoate, in the present study, is consistent with the results obtained from other studies where authors concluded that dosages of anticholinesterases which are not maternally toxic, do not produce embryotoxicity or fetotoxicity (Farag et al., 2000, 2003). It is noteworthy that foetotoxicity manifested as foetal death occurred only in the group that received 38 mg/kg of cypermethrin and 2.8 mg/kg of dimethoate and it was in this same treatment group that two dams exhibited signs of toxicity. It is pertinent to mention that all the previous studies referred to above, involved the use of doses of dimethoate far higher than the low doses used in the present study. In addition, those studies investigated dimethoate as a single pesticide and not in combination with other pesticides.

The present study also revealed that combined exposure to cypermethrin and dimethoate resulted in a reduction in the litter size. This is consistent with the reported effect of dimethoate exposure causing increased foetal resorption and reduced number of live foetuses (Farag et al., 2006). In the same vein, cypermethrin has been shown to also cause foetal resorption and reduced litter size (Madu, 2015).

Maternal co-exposure to cypermethrin plus dimethoate at the doses used in the present study, did not significantly alter litter weight of the fetuses. This shows that the pesticides at the doses used did not adversely

affect the foetus, since body weight alterations is a demonstration of stress exposure In addition, the exposure did not adversely affect the absolute and relative weights of the brain, kidneys, liver, lungs, spleen, uterus and ovaries of pregnant females in the control animals as well in the three treatment groups. However, the relative heart weight in animals exposed to 38 mg/kg cypermethrin + 2.8 mg/mg dimethoate these weights were significantly ($p < 0.05$) lower as compared to that of the animals in the control group. There was no evidence in the literature on the effects of either cypermethrin or dimethoate on the heart/body weight ratio. The fact that there was a significant change in the relative heart weight following exposure to 38 mg/kg cypermethrin + 2.8 mg/mg dimethoate showed that the heart is highly susceptible to injury provoked by the pesticides. The observed reduction in the relative heart weight in the present study may be due to some of the unknown untoward consequences of the interaction between cypermethrin and dimethoate following combined exposure, which had not been hitherto studied. We can however speculate that oxidative injury and/or direct cytotoxic damage to the heart provoked by the pesticide mixture may have been partly responsible for the lower relative heart weight in the present study.

The present study also revealed that maternal exposure caused increased foetal resorption, similar to what was observed following dimethoate (Farag et al., 2006) and cypermethrin (Raees et al., 2010; Madu, 2015) exposure. Exposure to xenobiotic such as dimethoate and cypermethrin that eventually disrupt ovarian steroid secretion would directly result in inadequate uterine decidualization and receptivity (Matt and Borzelleca, 1995). Fetuses were often susceptible to toxicant due to their fragile developmental state and lack of adequate defense mechanisms (Kimberly et al., 2004). Also, the complex nature of the reproductive regulatory process allows for numerous target sites and accounts for the various mechanisms through which toxins operate to exert their adverse effects (Abouamer et al., 2013).

Sex ratio, defined as ratio of number of males to females has been shown to decrease in the groups exposed to the pesticide mixture in the present study, indicating bias towards female sex. Studies have revealed a decrease male to female ratio following maternal exposure of rats to dimethoate (Abouamer et al., 2013) and cypermethrin (Huang and Li, 2014). Garry et al. (2002) have also reported a decrease in sex ratio of children born to pesticide applicators. A trend towards a declining proportion of male births has been noted in many industrialized countries (Astolfi and Zonta, 1999) and many factors including widespread use of environmental endocrine disrupting chemicals such as pesticides have been implicated (Martuzzi et al., 2001). Therefore, the sex ratio alteration in favour of females recorded in the present study may be linked to endocrine disrupting properties of the insecticide mixture.

In conclusion, the present study has shown that maternal co-exposure to diemethoate and cypermethrin even at low doses do adversely alter some maternal and foetal parameters, and therefore, restriction of pregnant mother to pesticide exposure is quintessential to promoting child health.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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