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Self-reported Health Effects among Short and Long-term Pesticide Sprayers in Arusha, Northern Tanzania: A cross Sectional Study

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Abstract

Background: The aim of the present study was to assess whether long-term exposure to pesticides is associated with adverse health effects in professional pesticide sprayers.

Methods: The study was conducted in Lake Eyasi Basin and Ngarenanyuki in Arusha region, during the dry season in September-October 2013. In a cross-sectional study, 97 short-term exposed men with at most three months as professional sprayers were compared with 60 long-term exposed men with experience of at least five years as professional sprayers. The study participants were aged 18-30 years, drawn from the same source population and interviewed using semi structured questionnaire. The questions focused on spraying procedures and on present and recurrent medical history including presence of selected six known pesticide induced health conditions.

Results: Organophosphates, carbamates, dithiocarbamates and pyrethroids were the most applied insecticides but also organochlorine fungicides and endosulfan were frequently applied. The majority of the sprayers reported unsafe pesticide use. Mean pesticide uses in litres, spray frequency per crop and per week were 637, and 1.3 respectively for about 270 days a year. Respiratory disease symptoms were the most frequently reported (46/157; 29.3%) followed by skin (27/157; 17.2%), and sight (24/157; 15.3%). When adjusted for age and other predictors, long-term exposed sprayers had significantly higher self-reported occurrences of peripheral neuropathy (OR=7.7, CI95%: 1.045-56.728, p=0.045) and respiratory disorders (OR=0.2, CI95%: 0.067-0.501, p=0.001) compared with short-term exposed. Furthermore, 10 sprayers, all long-term exposed reported poor libido and erection problems. **Conclusions:** These findings document lack of safety knowledge, safe pesticide management and the implementation of protective measures as well as suggesting that long-term exposure to pesticides increase the risk of experience disease conditions compared to short-term exposure.

Keywords: Exposure duration; Pesticides; Sprayers; Self-reported disease

Introduction

Pesticides are toxic chemicals used to protect crop against insects, other organisms harmful to cultivated plants including weeds thereby increasing crop yields and efficiency of food production. There are more than 1000 active ingredients, which are marketed as pesticides [1], and developing countries use 25% of the annual global consumption [2]. In Tanzania, a total of 300 active ingredients were registered and used by 2006 [3], including endosulfan, which is restricted by the Stockholm Convention due to its environmental persistence and the documented toxic potential [4]. Furthermore, the Tanzanian pesticide import increased from 500 to 2500 tonnes between 2000 and 2003 and the Arusha region, which is the study location of the present study, is one of the heavy pesticide users in Tanzania .

To control the trade and use of pesticides, Tanzania has developed a regulatory framework, adopted from the UN Food and Agriculture Organization (FAO), which aims to ensure best practices when using pesticides. Tanzania has also ratified the Stockholm convention, a global treaty under the United Nation Environment Program (UNEP), for protecting humans and environment from continued exposure to persistent Organic Pollutants (POPs).

However, despite the establishment of regulatory frameworks, a high degree of misuse among farmers are reported including over- and under-dosing, mixing of different pesticides, dangerous storage of pesticide and spraying equipment and poor use of personal protective gears [5]. Available data demonstrating unsafe pesticide handling practices in Tanzania suggest a high potential for human exposure, with the highest risk of occupational exposures among pesticide sprayers, farmers, and other agricultural workers. Accordingly, previous Tanzanian *questionnaire*-based *studies* identified unsafe pesticide use associated with acute pesticide poisoning as a major problem in the farming community [6,7]. Modern pesticides are reported to cause acute health effects in respondents exposed to high doses with unspecific symptoms such as headache, dizziness, respiratory problems, nausea, vomiting and eventually death. Furthermore, the data addressing potential adverse effects of long-term exposure to moderate pesticide levels suggest a wide variety of adverse health conditions, including central nervous-, reproductive- and immune system disorders, as well as cancers [8-21].

There is also circumstantial evidence on the association of exposure to pesticides with chronic diseases like respiratory problems, dermal disorders, cardiovascular disease, nephropathies, chronic fatigue syndrome and aging [1]. Since health-workers are not adequately trained to identify adverse effects of pesticides [22,23] and because of the

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unspecific symptoms related to exposure to pesticides [24], a substantial underreporting of pesticide induced health effects is suspected in Tanzania and other developing countries [25]. In addition, the Health Management Information System (HMIS) in Tanzania has only one category for all cases of poisoning, reflecting a lack of comprehensive registry of adverse health effects associated with exposure to pesticides. Thus, studies which provide scientific based evidence documenting a link between unsafe pesticide-use and adverse health effects in Tanzania and other developing countries, is strongly needed for the initiation of interventions and outreach to improve public health.

In the study area, pesticides are applied to more than 5000 hectares farmland for more than 270 days between January and September each year. Among the professional sprayers there is a widespread praxis of poor pesticide handling such as improper storage, mixing several pesticides, bare hands loading, unhygienic spraying, lack of protective equipment use as well as haphazard disposal [26] of remnants and empty containers. The excess use of pesticides coupled with inadequate personal protection, is likely to increase the exposure dose among sprayers in the area [27]. Despite the contribution of these pesticides in improving agricultural production and protection of the harvests, they threaten the human health as a result of poor protection and indiscriminate use and handling [28].

Even though the first reports about extensive use and misuse in Tanzania were published for more than a decade ago, very few studies have assessed acute toxic effects while no studies have assessed association between long-term exposure to pesticides and adverse health effects. The main aim of the present study was to assess practice of pesticide use on farms and to assess potential associations between exposure duration and self-reported pesticide induced diseases among pesticide sprayers.

Materials and Methods

Time and study setting

Data were collected in dry season from 9 AM to 12 noon, Monday through Friday, between September and October of 2013 at health facilities in Ngarenanyuki along tomato and Mang'ola along onion farms in Arusha. It was warm with strong winds and with temperatures around 19°C, sometimes warmer and during day time up to 34°C. In these areas, onion and tomato farming is the major economic and subsistence activity. The sprayers were interviewed in the doctor's consultation room at the health facility. The room was quiet, with adequate privacy and a comfortable environment. The potential participant was asked to either accept or reject at reception desk at the health facility to participate in responding to occupational questions for at least 10 minutes after identifying himself occupationally as a sprayer-farm worker and after informed consent.

Recruitment

The study respondents were male farm workers involved in spraying onion and tomato farms using pesticides. They were recruited at outpatient clinic when escorting female partner or a child at pregnant women or child growth monitoring clinic respectively. The recruitment of a sprayer was based on the duration of time he had worked as sprayer, and was categorized as either short-term exposed or long-term sprayer. The short-term exposed sprayers were used as the contrast group, each with a history of regular spraying activity for 3 months or less. The long-term sprayers were farm workers involved in spraying for at least 5 years. Those that had history of smoking, taking alcohol, hypertensive, worked for more than 3 months but less than 5 years as sprayers were not recruited. Residential but seasonal sprayers were excluded, as well as individuals who had been diagnosed with diabetes, liver or kidney disease, or peripheral neuropathy before starting work as a sprayer were also excluded. The purpose of the research was explained to potential study respondents at each of the two health facilities' outpatient departments, and those who consented to a questionnaire interview were recruited. The consent form used was reviewed and approved together with ethical clearance by the Medical Research Coordinating Committee of the National Institute for Medical Research.

Exposure levels

Sprayers exposed for at least 5 years were defined as exposed (high exposure level) and the short-term exposed sprayers were defined as baseline or unexposed (low exposure level or contrast group) for comparison. The occurrence of pesticide-induced self-reported adverse health effects was proportionally explored using these two groups.

Sample size

Using the formula by Kelsey et al. (2007), the cross-sectional study required a total minimum of 118 sprayers. In a ratio of 1:1, 59 long-term and 59 short-term exposed sprayers were required as adequate representative sample for each subgroup to provide power of study of 80% at an estimated level of disease symptoms 50% and 25% in long-term and short-term exposed sprayers, respectively. This calculation was based on a significance level of $\alpha=0.05$. In the field the data were collected from 157 sprayers, of whom 97 were short-term exposed and 60 long-term sprayers.

Questionnaire and definition of self-reported disease conditions

The questions focused on social and personal information, past and present medical history including whether there were pesticide induced health conditions among interviewees. The present study limited itself to neurologic, sight, skin, and heart, respiratory and reproductive and sexual complaints as a scope of conditions. All symptoms were defined and listed in the questionnaire for a selected provisional diagnosis the sprayer had. The peripheral neurological disease condition was defined if the respondent had experienced numbness, tingling, burning sensation of hands and or feet, and vision problem if had not been able to see properly, with no symptom of eye infection associated with pain. For skin disease condition was defined if he had rash, irritation/itching, eczematous reaction, or skin colour change, and for cardiovascular disease condition if he was told to have high blood pressure, or any heart problem diagnosis at health facility. A respiratory disease condition was defined by presence of wheezing, chest tightness, cough whereas sexual or fertility dysfunction if he had not been able to make babies for at least a year of unprotected sexual intercourse and if the respondent had erection problems.

Data collection and statistical analysis

Before data collection the questionnaire was pre tested and improved accordingly at Momella dispensary in Ngarenanyuki using 10 farm workers that came for outpatient clinic services. These were not included in data entry and analysis. The semi-structured questionnaire with mainly closed ended questions was administered in the doctor's consultation room by the investigator and an experienced, clinical medicine diploma holder that was specially trained for the present study. The respondents were asked about names and quantity of pesticides they used, quantity used per acre and frequency of spraying per crop and week. They were also asked whether they used personal protective equipment such as mask, hat, gloves, shoes, glasses etc. The pesticide sprayers with experience ≤3 months were defined as short-term sprayers and coded 0 and sprayers with experience of ≥5 years were defined as long-term sprayers and coded 1. Thus, exposure variables included: Exposure duration (short and long-term: coded 0, 1) in occupation as a sprayer, age, spray frequency per week, spray frequency per crop, litres of pesticides applied per acre (as continuous variables). The responses whether the sprayer used protective devices were either no or yes which were coded as 0 or 1 respectively. The outcome variables were responses about self-reported symptoms clinically classified as peripheral neurological, visual/sight, dermatological/skin, respiratory and reproductive/sexual health disorders as dichotomous choices. After descriptive uni and bivariable group comparisons using a student t-test for continuous variables and the chi square test for categorical variables, finally, a multivariable logistic regression was performed to statistically adjust for age as a potential confounding variable along with exposure duration to predict selected possible pesticide induced disease (0=absent; 1=present). The variables included in the model as predictors were age, exposure duration, spray history, litres of pesticides applied per acre, frequency of spray per crop and per week. All statistical analyses were performed using Stata v12 (SE 11 for Windows, StataCorp LP, College Station, TX).

Results

Respondent characteristics, pesticide use and potential exposure

The interviewed 157 men sprayers were at an average of 24 years (range 18-30), with 51.6% (81) from Ngarenanyuki (tomato farms) and 48.4% (76) from Mang'ola (onion farms). About two third, 62.6% (97) were short-term exposed sprayers and 37.4% (58) were long-term sprayers. The mean age of the short-term exposed group was 22.7 ± SD of 3.9 and 25.5 ± SD of 3.4 years ($p<0.01$) for long-term sprayers. Out of 60 interviewed long-term sprayers, information about duration in occupation for two individuals was missing; they were therefore removed from analysis. The long-term exposed sprayers applied significantly more pesticides per acre per spray visit ($p=0.005$; mean 720 l) compared to the short-term exposed sprayers (mean 580 l). However, the long-term exposed group had significantly ($p<0.001$) lower mean frequency (mean 7 times versus 10) of spraying per crop during the growing season, whereas the difference of spray frequency per week was not significant between the two groups as shown in Table 1.

Applied pesticides including organophosphates, carbamates, pyrethroids were mainly class II, WHO hazard classification. More than 20% of the sprayers also used the internationally banned organochlorine endosulfan (https://en.wikipedia.org/wiki/Stockholm_Convention_on_Persistent_Organic_Pollutants). Furthermore, application of fungicides included triazoles (triadimefon), dithiocarbamates (mancozeb) and organochlorine (chlorothalonil). About half (49.4%), more than three quarters (85.1%) and about a quarter (23.4%) of the sprayers applied triadimefon, mancozeb and chlorothalonil among tomato sprayers respectively either single or combined formulation. At times they used the same ingredients in one container due to different brand names. The majority of the sprayers reported that they used to mix several pesticides for spraying and that more than 90% wore no personal protective devices at work. Table 2 shows the applied pesticides by brand names, active ingredients, mechanisms of action and the number and percentages of users. When asked to discriminate the pesticides they used, 12/157 (7.6%) and 28/138 (20.3%) of sprayers misclassified by giving incorrect responses between insecticides and fungicides respectively. Furthermore, 135/155 (87.1%) and 145/157 (92.4%) reported that they did not use any personal protective equipment for head and trunk skin, respectively.

Self-reported disease symptoms

Symptoms related to respiratory disease such as wheezing and coughing were the most frequently reported (46/157; 29.3%). In addition, peripheral neurological, sight, skin, heart and sexual health symptoms were reported by 5.1%, 15.3%, 17.2%, 5.1% and 6.4% respectively. Table 3 summarizes the multivariable logistic regression odds ratios (OR) and CI 95%. The logistic regression analyses showed that peripheral neuropathy (OR=7.7; CI95%: 1.05-56.7) and respiratory disorders (OR=0.2; 0.07-0.50) were significantly higher in sprayers with short-term exposure to pesticides compared to those with long-term exposure. The sight problem was significantly associated with quantity of pesticides a sprayer applied (OR=1.03; 1.01-1.07). Furthermore, 10 respondents, all of them from long-term exposed sprayers reported that they had sexual function problems, mainly erectile dysfunction and lack of libido. In particular, eight reported poor libido and erection as the problems whereas two of the respondents declined to specify their sexual function problem during the interview. Using exact logistic regression the results show a significant prediction of exposure duration on having a sexual health problem (OR=20.0; 3.1-infinity) among long-term exposed sprayers.

Although skin and heart related symptoms were not significantly different between the two exposure groups the level of skin problems was high in both the short-term and long-term exposed sprayers. The percentage of skin problems among the short-term exposed sprayers was 15.0% whereas the percentages for the long-term exposed was 20.7%. The occurrence of heart related symptoms were 3.1% short-term and 8.6% long-term exposed sprayers. A significantly ($p=0.048$) higher proportion (18/58; 31%) of the long-term exposed sprayers reported two or more pesticide disease conditions compared to (14/97; 14%) among short-term exposed sprayers. The majority of the short-term exposed sprayers were either free from any disease symptoms or had one (83/97; 86%) disease condition compared to long-term exposed sprayers (40/58; 69%) during the study period.

More than a quarter (26.2%, 32/122) of sprayers discretionally considered pesticides to influence the adverse health effects occurrence. The majority (91.6%; 141/154) of sprayers either agree or strongly agree that long-term exposure to pesticides might have long-term health effects to applicators as detailed in the Table 4. Table 5 shows the distribution of yes and no responses of the six pesticide induced disease conditions and their recurrence statuses among the two comparison groups. Peripheral neurologic and sexual health problems were significantly higher in the long-term exposed sprayers compared to short-term sprayers except for respiratory problems which were higher in the short-term exposed sprayers. However, the differences of sight, skin, and heart symptoms were not significant among the two groups of exposure duration.

Self-reported disease condition recurrences

When those who reported peripheral neurologic and sight problems were asked about recurrence of their condition, more recurrence was shown in the long-term compared to short-term exposed sprayers, with 87.5% compared to 12.5% for peripheral neurologic problems whereas 92.3% compared to 7.7% for sight problems. Among those who reported respiratory problems, a more recurrence was shown in the short-term exposed (64%) compared to long-term exposed sprayers (36%).

Table 1a. Frequency distribution of exposure groups, exposure history, practice characteristics of sprayers

Variable	Number (n) of respondents	Category variable	Number of counts (%)	p value
Exposure duration	155	≤ 3 months	97 (62.6)	N/A
		≥ 5 years	58 (37.4)	N/A
Have you been working as a pesticide sprayer in the farms before coming to this area?		No	135 (87.1)	N/A
	155	Yes	20 (12.9)	N/A
How many knapsacks of pesticides do you usually apply per acre every time you spray?		≤ 375 litres	78 (50)	N/A
	156	> 375 litres	78 (50)	N/A
How many times is the crop sprayed from planting till harvest?		< 11 times/crop	79 (50.6)	N/A
	156	≥ 12 times/crop	77 (49.4)	N/A
How many times do you usually expose yourself through mixing, loading and spraying in a week?		≤2 times/week	141 (92.8)	N/A
	152	≥ 3 times/week	11 (7.2)	NA
Do you protect yourself by wearing PPD against inhaling (nose, mouth) pesticide when mixing, loading and spraying?		No	135 (87.1)	N/A
	155	Yes	20 (12.9)	N/A
Do you protect yourself by using wearing PPD against touching (hands, face/head, foot and trunk) pesticide when mixing, loading and spraying?		No	145 (92.4)	N/A
	157	Yes	12 (7.6)	N/A

1b. Practice characteristics of new entry and long-term exposed sprayers compared (bivariate analysis)

Categorized variables	Number (n) of respondents	≤ 3 months n (%)	≥ 5 years n (%)	p value
Apply ≤ 375 litres per acre (n=78)		61 (78.21)	17 (21.79)	<0.001
Apply > 375 litres per acre (n=76)	154	35 (46.05)	41 (53.95)	
Spray frequency per crop ≤11 (n=77)	154	33 (42.86)	44 (57.14)	<0.001
Spray frequency per crop ≥12 (n=77)		63 (81.82)	14 (18.18)	
Spray frequency per week ≤2 (n=139)	150	89 (64.03)	50 (35.97)	0.22
Spray frequency per week ≥3 (n=11)		5 (45.45)	6 (54.55)	
No mouth protection when spraying (n=133)		84 (63.16)	49 (36.84)	0.785
Protect mouth when spraying (n=20)	153	12 (60)	8 (40)	
No skin-trunk protection when spraying (n=143)	155	90 (62.94)	53 (37.06)	0.752
Protect skin-trunk when spraying (n=12)		7 (58.33)	5 (41.67)	

1knapsack=15 litres of pesticides; PPD=Personal protective devices

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1knapsack=15 litres of pesticides; PPD=Personal protective devices

Table 1: Exposure history, characteristics of study respondents and their occupational practice as sprayers

	Pesticide type (activity)	Brand name known by users	Active ingredients	Chemical classification name	Mechanism of action	Pesticide mentioned and used n (%)	Use of pesticide category aggregate* in %
Onion list of pesticides as mentioned by sprayers (users=76)	Insecticide	Marshal 250EC	Carbosulfan	Carbamate	Neurotoxin, inhibition of acetylcholinesterase (reversible)	75 (98.7)	98.7
	Insecticide	Selecron 720EC	Profenofos	Organophosphate pesticides	Neurotoxin, inhibition of acetylcholinesterase (irreversible)	22 (29.5)*	38.8
	Insecticide	Dursban 24ULV	Chlorpyrifos	Organophosphate pesticides	Neurotoxin, inhibition of acetylcholinesterase (irreversible)	4 (5.3)*	
	Insecticide	Bamiphos 500EC	Pirimiphosmethyl	Organophosphate pesticides	Neurotoxin, inhibitor of acetylcholinesterase (irreversible)	3 (4.0)*	
	Insecticide	Thionex 35EC	Endosulfan	Organochlorine	Neurotoxin, inhibitor of GABA gated chloride channel receptor (preventing chloride flux across membranes) thereby paralyzing the organism	7 (9.2)**	17.2
	Insecticide	Karate 5CS, Decis 25EC, Ngao	Lambda-cyhalothrin, Deltamethrin,	Pyrethroids	Neurotoxin, axonic excitoxins, by closure prevention of voltage-gated Na+ channel in axonal membranes	4 (5.3)***	73.8
	Acaricide and insecticide	Dipu (Alfanex 10%EC and Alphaguard 0.8ULV)	Alpha-cypermethrin	Pyrethroids	Neurotoxin, axonic excitoxins, by closure prevention of voltage-gated Na+ channel in axonal membranes	3 (4.0)***	
	Combined insecticides	Polytrin P 440EC, Duduba 450EC	Profenofos + cypermethrin, Chloropyrifos +cypermethrin	Organophosphate pesticides plus pyrethroids	Neurotoxin, inhibition of acetylcholinesterase (irreversible), Plus neurotoxin, axonic excitoxins, by closure prevention of voltage-gated Na+ channel in axonal membranes	18 (23.7)* 31 (40.8)*/***	64.5
	Fungicide	Blue copper	Copper sulphate	Copper fungicide	Disrupts cellular proteins	48 (63.2)	63.2
	Combined fungicide	Banko Plus	Chlorothalonil + Carbendazim	Organochlorine	Multisite inhibitor of enzymes and metabolic processes (reduces intracellular glutathione molecules to alternate forms)	6 (8.0)**	8.0
Tomato list of pesticides as mentioned by sprayers (users=81)	Insecticide	Selecron 720EC	Profenofos	Organophosphate pesticides	Neurotoxin, inhibitor of acetylcholinesterase (irreversible)	5 (6.2)*	76.5
	Insecticide	Dursban 24ULV, Twigaphos 48EC	Chlorpyrifos	Organophosphate pesticides	Neurotoxin, inhibitor of acetylcholinesterase (irreversible)	23 (28.4)* 13 (16.0)*	
	Insecticide, acaricide	Dume 40EC, Twigathoate 40EC	Dimethoate	Organophosphate pesticides	Neurotoxin, inhibition of acetylcholinesterase (irreversible)	6 (7.4)*	

	Insecticide, acaricide	Thionex 35EC	Endosulfan	Organochlorine	Neurotoxin, inhibits GABA gated chloride channel receptor (preventing chloride flux across membranes) thereby paralyzing the organism	6 (7.4)**	30.8
	Insecticide	Ninja 5EC, Karate 5CS	Lambda-cyhalothrin	Pyrethroid	Neurotoxin, axonic excitoxins, by closure prevention of voltage-gated Na+ channel in axonal membranes	18 (22.2)*** 12 (14.8)***	64.2
	Insecticide, acaricide, nematicide	Abamectin 20EC, Vertigo 1.8EC	Abamectin	Avermectin	Neurotoxin, stimulats the release and binds gamma-aminobutyric acid (GABA) at nerve endings thereby causing irreversible paralysis of the neuromuscular systems	51 (63.0)	63.0
	Insecticide, acaricide	Appolo	Clofentezine		Inhibits embryo development, non specific mode of action (mite growth inhibitor)	2 (2.5)	-
	Combined insecticides	Duduba Dudu all	Chlorpyrifos + cypermethrin	Organophosphate pesticides plus pyrethroids	Inhibitor of acetylcholinesterase (irreversible) plus neurotoxin, axonic excitoxins, by closure prevention of voltage-gated Na+ channel in axonal membranes and neurotoxin,	13 (16.0)* 14 (17.3)***	-
	Combined insecticides	Fenom plus, Fenom	Profenofos + Lambda-cyhalothrin, Profenofos + Cypermethrin	Organophosphate pesticides plus pyrethroids	Neurotoxin, inhibition of acetylcholinesterase (irreversible) plus neurotoxin, Axonic excitoxins, by closure prevention of voltage-gated Na+ channel in axonal membranes	2 (2.5)*/*** 5 (6.2)*/***	-
	Combined insecticides	Dudukill	Lambda cyhalothrin + Carbaryl	Pyrethroid plus carbamate	Neurotoxin, axonic excitoxins, by closure prevention of voltage-gated Na+ channel in axonal membranes plus neurotoxin, inhibitor of acetylcholinesterase (reversible)	3 (3.7)***	-
	Fungicide	Bayleton 250EC Bajuta	Triadimefon	Triazole	Triazole=inhibits the cyt P450 enzyme 14-alpha sterol-demethylase to arrest fungal growth	40 (49.4)	49.4
	Fungicide	Bravo, Linkonil	Chlorothalonil	Organochlorine	Chlorothalonil= Multisite inhibitor of enzymes and metabolic processes (reduces intracellular glutathione molecules to alternate forms)	12 (14.8)***** 3 (3.7)*****	23.4
	Fungicide	Antracol 70WP	Propineb	Dithiocarbamate	Propineb=Inhibits enzymes involved in lipid and protein metabolism and respiration	4 (4.9)****	85.1
	Fungicides	(Milthane super, Farmerzeb, Redofil) Mancozeb , Ivory 80WP, Oshothane 80WP,	Mancozeb	Dithiocarbamate	Mancozeb=Inhibits enzymes involved in lipid and protein metabolism and respiration	24 (29.6)**** 2 (2.5)**** 7 (8.6)**** 7 (8.6)****	
	Fungicide	Tankopa 500WP	Copper oxychloride	Multi-site inorganic copper	Disrupts the enzyme system function	3 (3.7)	-

	Combined fungicides	Ebony M72, Victory 72WP, Ridomil 68WG	Mancozeb + metalaxyl	Dithiocarbamate	Mancozeb=Inhibits enzymes involved in lipid and protein metabolism and respiration Metalaxyl= growth inhibitor, inhibits nucleic acid synthesis	21 (25.9)**** 2 (2.5)**** 2 (2.5)****	-
	Combined fungicides	Banko plus	Chlorothalonil + Carbendazim	Organochlorine + Benzimidazole carbamate	Chlorothalonil= Multisite inhibitor of enzymes and metabolic processes (reduces intracellular glutathione molecules to alternate forms) Carbendazim=inhibits fungal mitotic microtubule formation.	4 (4.9)*****	-
	Unknown	Vita†				3 (3.7)	3.7
	Unknown	Enabo†				3 (3.7)	3.7
†Not available in the list of registered pesticides by Tanzania Pesticide Regulatory Institute (TPRI), 2010.							
*Organophosphates; **Organochlorine insecticides; ***Pyrethroid insecticides; ****dithiocarbamates; *****Organochlorine fungicides							

Table 2: List of commonly applied pesticides by sprayers on onion and tomato farms in Mang'ola and Ngarenanyuki respectively.

Outcomes (disease condition)	Peripheral neurologic (n=155)		Sight (n=154)		Skin (n=154)		Heart (n=155)		Respiratory (n=155)		Sexual health (n=154)		Chronicity ≥ 3 months (n=12)	
predictors	Adj OR	CI 95%	Adj OR	CI 95%	Adj OR	CI 95%	Adj OR	CI 95%	Adj OR	CI 95%	Adj OR	CI 95%	Adj OR	CI 95%
Age in years	0.96	0.773-1.198	1.1	0.957-1.257	1.01	0.892-1.134	1.09	0.872-1.352	1.13	1.02-1.264	1.1	0.849-1.458	1.14	0.891-1.456
Exposure duration (ref, long)	7.7	(1.045-56.728)*	1.4	(0.504-4.104)	0.68	(0.241-1.891)	1.05	(0.152-7.271)	0.2	(0.067-0.501)*	1	-	12.4	(1.410-108.407)*
History of pesticide spraying before study area residency (ref, yes)	0.7	0.058-8.477	1.2	0.343-4.301	1.02	0.363-4.180	2.8	0.307-25.106	5.8	1.576-21.231	1.8	0.198-15.576	0.89	0.107-7.388
Quantity of pesticide in litres applied per acre	1.02	0.979-1.062	1.03	1.008-1.068*	0.99	0.964-1.021	0.9	0.850-0.978	0.99	0.960-1.012	0.99	0.946-1.038	1.03	0.988-1.076
Frequency of spray per crop	1.09	0.881-1.356	0.9	0.757-1.055	0.75	(0.620-0.903)*	0.7	0.512-0.939	0.88	0.761-1.026	0.9	0.692-1.215	0.95	0.761-1.191
Frequency of spray per week	1	-	0.53	0.245-1.141	0.5	0.192-1.279	1.2	0.535-2.651	0.5	0.209-1.068	0.9	0.400-1.846	1	-
*significant with p<0.05														

Table 3: The influence of exposure period to magnitude of selected known pesticide induced disease condition before and after age control by logistic regression.

	In your opinion, what do you think has influenced (caused) the occurrence of this condition to you? n=122			Do you agree that long-term exposure to pesticides might have long-term health effects to applicators? n=154			
Variable	Don't know	Exposure to pesticides	Weather changes	Strongly disagree	Disagree	Agree	Strongly agree
Exposure period	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
≤ 3 months	48 (65.8)	10 (31.3)	12 (70.6)	1 (50.0)	7 (63.6)	62 (68.1)	27 (54.0)
≥ 5 years	25 (34.3)	22 (68.8)	5 (29.4)	1 (50.0)	4 (36.4)	29 (31.9)	23 (46.0)

Table 4: Respondents perception on the probable cause of their long-term disease conditions in the study area.

Discussion

In the present study, self-reported peripheral neuropathy and sexual health symptoms were significantly associated with long-term pesticide exposure. In contrast, the respiratory symptoms were significantly higher in the short-term exposed compared to long-term exposed. Although no difference in sight and skin symptoms were noted at the interview time, a higher occurrence was reported by the long-term exposed when asked whether their symptoms were chronic. Although the mean age was lower in the short-term exposed group, the difference showed no significant contribution to disease occurrence when adjusted for age in the regression model. Age ranged from 18 to 30 years in both comparison groups. This reflects that long-term use and handling of pesticides increase the exposure risk and may increase

Do you have an XX disease condition at the moment? Table 1						Do you have recurrent XX disease condition at the moment?				
			Short-term exposure	Long-term exposure				Short-term exposure	Long-term exposure	
Disease condition (Respondents)	Subtotal, respondent categories	Response	≤ 3 months n (%)	≥ 5 years n (%)	p value	Recurrent conditions (variable)	Response	≤ 3 months n (%)	≥ 5 years n (%)	p value
Peripheral neurologic (n=155)	147	No	95 (64.6)	52 (35.4)		Neurologic (n=11)	No	1 (33.3)	2 (66.7)	
	8	Yes	2 (25.0)	6 (75.0)	0.024		Yes	3 (37.5)	5 (62.5)	0.046
Sight (n=154)	130	No	85 (65.4)	45 (34.6)		Sight (n=24)	No	8 (88.9)	1 (11.1)	
	24	Yes	12 (50)	12 (50)	0.155		Yes	3 (20.0)	12 (80.0)	0.001
Skin (n=154)	127	No	81 (63.8)	46 (36.2)		Skin (n=27)	No	11 (68.7)	5 (31.3)	
	27	Yes	15 (55.6)	12 (44.4)	0.537		Yes	3 (27.3)	8 (72.7)	0.045
Heart (n=1550	147	No	94 (64.0)	53 (36.1)		Heart (n=9)	No	2 (100)	0 (0)	
	8	Yes	3 (37.5)	5 (62.5)	0.132		Yes	2 (28.6)	5 (71.4)	0.122
Respiratory (n=155)	109	No	62 (56.9)	47 (43.1)		Respiratory (n=44)	No	15 (79.0)	4 (21.0)	
	46	Yes	35 (76.1)	11 (23.9)	0.024		Yes	18 (72.0)	7 (28.0)	0.139
Sexual health (n=154)	146	No	97 (66.4)	49 (33.6)		Sexual health dysfunction (n=154)	NA	97 (66.4)	49 (33.6)	
	8	Yes	0 (0)	8 (100)	< 0.001		Impotence	0 (0)	4 (100)	_
If the condition is long-term (at least≥ 3 months), If Yes, how long do you have this problem till now? (n=122)	111	No	69 (62.2)	42 (37.8)			Loss of libido	0 (0)	4 (100)	
	11	Yes	2 (18.2)	9 (81.8)	0.005					
Pearson chi² and Exact tests applied accordingly, significant/different at p=0.05, where NA=Not applicable										

Table 5: Association between exposure duration (short-term or long-term) and selected known pesticide induced disease conditions and whether they were recurrent.

the risk of adverse health effects. Occupational exposure to pesticides among sprayers associated with increased occurrences of disease symptoms in the study area may be predictive of a potential range of health problems beyond the results of this study.

In the present study, the disease conditions reported by pesticide sprayers including neurologic, sight, skin, heart, respiratory, reproductive and sexual health were assessed. Each disease condition was identified using a list of certain criteria of symptoms that the sprayer was able to identify. Such symptoms were numbness and or burning or tingling sensation of either hands and or feet for peripheral neuropathy [20], wheezing, cough, chest tightness [29] without feeling high body temperature as respiratory disorder, skin reaction by itching, irritation, rashes, change of colour or eczematous reaction [30]. Visual performance not related to eye infection was defined as sight problem [31]. Heart problem included being diagnosed as hypertensive or any diagnosis related to heart problem at hospital. When asked about whether they had experienced reproductive and sexual problems the sprayers reported no reproductive but sexual health problems, these were impotence and libido.

A variety of adverse health effects associated with pesticide exposure is reported in humans [32-34]. However, the present study was limited to a scope of six selected disease conditions that have been associated with pesticide exposure in previous reports. The present study showed that long-term exposure to pesticides increased the risk of peripheral neuropathy conditions about eight times compared to short-term exposure. This finding is in line with previous data [8,35,36] which show association between peripheral neuropathies and chronic exposure to pesticides. Furthermore, endosulfan, which is banned in many countries due to its persistence and bio-accumulative properties, was used by more than 20% of the study participants. Endosulfan together with other modern pesticides that are frequently applied in the study area are likely to induce neurotoxic as well as other toxic effects in chronically exposed humans as previously described [37-39]. It is well documented that the nervous system represents a key target for both acute and chronic effects of pesticides [9,20]. Groups of pesticides with known effect on the nervous system include organochlorines, pyrethroids, organophosphates and carbamates. These compounds have the potential to alter neurological functions by interacting with among other mechanisms, sodium and chloride channels activity (pyrethroids) and/or inhibiting the acetylcholinesterase (AChE) (organophosphates and carbamates). The AChE is essential enzyme for normal nerve conductivity throughout the central and peripheral nervous systems and any disturbance of AChE activity may lead to a variety of acute symptoms such as confusion, convulsions, weakness, loss of muscle control, respiratory paralysis etc, and chronic symptoms including polyneuropathy and neurodevelopmental effects. Of specific concern is whether pesticides have the potential to affect normal neurodevelopment, since the nervous system is known to be most susceptible to harm during development. Developing individuals may be exposed during fetal life and via breast milk as a result of maternal exposure and directly by unintended contact with pesticides. However, the potential effects of chronic, low-dose pesticide exposures on neurodevelopment remain uncertain suggesting a need for assessing neurologic conditions among the children in the area.

Surprisingly, the present study found a higher frequency of respiratory disorder symptoms among the short-term compared to the long-term exposed sprayers. The lower frequency of respiratory problems among the long-term exposed may be explained by adaptation and tolerance. Salameh et al. [40] showed that inhalation of pesticides induced irritation of the airways *causing* acute mucosal hyperactivity. However, individuals undergoing chronic exposure to the same irritants may develop tolerance by desensitizing the airways [41,42]. This could further be explained by cross-desensitization of reactive irritants to each other's ability to initiate respiratory defensive responses [42]. For example, rats chronically exposed to formaldehyde vapours developed reduced respiratory responses to subsequent exposures to acetyldehyde, and vice versa *[43]. A suggested explanation for this phenomenon is* that sensory neurons contain a single reactive irritant receptor site. Once this receptor site is saturated through exposure to an irritating chemical, it is rendered unresponsive to subsequent exposures by the same, or other, irritants [42].

The present study showed that exposure to modern pesticides including endosulfan for several years is associated with sexual health problems expressed in form of impotence and loss of libido. These findings are in line with previous reports [14,44] in which individuals that were regularly exposed to c*arbamates and endosulfan* reported reproductive and erectile dysfunction. In addition, Burnett [45] in his review reports increased erectile dysfunction and loss of libido in men exposed to a variety pesticides [46,47].

In a British study, impaired erectile function in four farm workers, who had used pesticides for over a 1-year [48] was documented. Pesticides including OPs were identified as harmful agents and it was suggested that these chemicals disrupted testosterone metabolism [49]. An interesting observation was that all four men recovered upon discontinuing their occupational activity. Another study assessed the erectile dysfunction risk in agricultural and industrial workers in Argentina [50]. The investigators found an increased risk (OR=8.4) of erectile impairment in the agricultural workers chronically exposed to pesticides with median exposure times of 12 years. Furthermore, an epidemiologic study among 208 Egyptian pesticide formulators and 172 pesticide applicators, who responded to standardized health questionnaires, showed higher rates (26.9%) of erectile dysfunction than the matched controls (4.2%). Among the pesticide formulators, exposed to pesticide for 40 hours per week, a positive association was found between exposure time (5 versus 20 years of exposure) and erectile dysfunction. In addition, both pesticide formulators and applicators showed significantly higher rates of psychiatric disorders than controls [47]. Various groups of pesticides (organophosphates, carbamates, pyrethroids) are known to produce toxic effects by affecting normal nerve conduction in the central and peripheral nervous systems [11]. Thus, pesticides can impair the neurogenic mechanisms involved in penile erection as well as other functions in the nervous systems. Although not directly shown for pesticides, induction of peripheral sensory-motor polyneuropathy and erectile dysfunction were diagnosed in a patient occupationally exposed to methyl bromide for 12 years [51] suggesting that neurologic mechanisms may be involved in erectile problems of the long-term exposed users.

In the present study, higher frequency of poor libido was found in long-term exposed compared to the short-term exposed sprayers. There are scant data available from previous studies on association between exposure to pesticides and reduced libido in humans. However, one study reported gynacomastia and loss of libido among Haitian refugees, who used the pyrethroid, phenothrin as a delousing agent. In that study, phenothrin was identified as an anti-androgen by competing with binding sites for testosterone in rat prostate tissues [52]. Testosterone hormone has stimulatory effect and thus, it remains an important determinant of sexual desire in men [53]. A review by Basson documents that testosterone therapy intensifies sexual desire in men as well as in postmenopausal women with reduced libido [54]. It is known that l*ibido* and *male* sexual behaviour are under the control of complex *testosterone*-dependent neuro-endocrine *mechanisms [55], suggesting that interplay of testosterone disturbance, neurotoxicity and endocrine disruption may affect libido. Thus, pesticides can affect libido and erectile function in humans by* blocking spontaneously uncontrollable sexual pulsions of testosterone secretion and consecutively decreasing androgen effects on target cells [55].

In the present study the occurrence of self-reported vision complaints was significantly higher in those who applied higher quantity of pesticides per spray event. A review by Jaga and Dharmani [56] documents that, exposure to pesticides as a function of dose-response relationship is associated with various ocular disorders such as retinal degeneration, optic neuritis, myopia, astigmatism, narrowed visual field etc. Because the sprayers in the present study did not use eye protection, it is likely that the eyes were directly exposed to substantial concentrations of pesticides including OPs. Because exposure to OPs has been associated with *loss of* cholinergic neurons in the brain and ocular pathways leading to permanent damage of *vision [57] it is likely that similar lesions may occur in the study participants of the present study.* This suggests that, substantial unrecognized vision disorders due to pesticide exposure may exist among pesticide sprayers as well as other farm workers in the study area.

Skin problems were frequently reported in sprayers regardless of varying exposure duration. Literature documents that chemical dermatitis is one of the most common occupational diseases [58] in humans. Different pesticides associated with adverse skin conditions reported by previous studies include carbaryl, chlorpyrifos, dimethoate, cypermethrin, lambda cyhalothrin and mancozeb. The study participants reported frequent use of all these pesticides in substantial amounts. Thus, unprotected exposure to relative high quantities of these pesticides, are likely to induce skin lesions in both long-term and short-term exposed sprayers.

In the present study dithiocarbamates and organochlorine fungicides (chlorothalonil) are frequently applied and in higher quantities among tomato compared to onion growers. Although these pesticides are not implicated in of acute toxicity and adverse health effects with long-term exposure they are reported to be associated with endocrine disruption in humans. Furthermore, chlorothalonil as an irritant to respiratory system is also suspected to be a human carcinogen (http://nj.gov/health/eoh/rtkweb/documents/fs/0415.pdf).

In the present study, various adverse health effects were documented among professional pesticide sprayers, who demonstrated poor knowledge, attitude and practices related to pesticide use. However, when considering the multitude of pesticides available at the market and that instructions are typically written in English language, incidences of misuse are very likely. For example, frequent misclassification of insecticides as fungicides and vice versa observed among the sprayers indicates a serious lack of knowledge. Poor practice is further exemplified by the common practice to mix several pesticides with different brand names containing the same active ingredients, which may lead to overdosing, Furthermore, the study participants spray from 8 AM to 1 PM without using personal protective devices, thereby exposing themselves to levels which may exceed the safe daily doses. Even though, poor knowledge, attitude and practices among Tanzanian farm workers were documented by Ngowi et al [23] for more than ten years ago, the present study was not able to demonstrate any improvements during this time period.

Several limitations of the present study should be noted. Because of limited resources, we had to restrict the present number of participants. The use of self-report data to assess disease condition may be inaccurate because the study participants might report what they believe reflects positively on their own abilities, knowledge or opinions. Another question is whether subjects are able to accurately recall past experiences. Furthermore, a cross sectional study design upon which these results are based is relatively weak in establishing causal effect relationship, hence weak evidence for causality. A detailed well designed study may disclose additional and more important biological information. However, despite the study limitations, the data obtained in the present study suggest association between increased risk of various disease conditions and long-term exposure compared to short-term. Furthermore, the observation of high levels of respiratory and skin problems among both long-term and short-term exposed sprayers, suggest increased risk of this disease conditions regardless of exposure time.

Conclusions

Safe pesticide use and handling including use protective measures were limited in the study area. In addition, unsafe practice with pesticides increases exposure risk and the occurrence of self-reported adverse effect. The higher levels of self-reported adverse health effects are observed among long-term compared to short-term exposed individuals. Chronic exposure to pesticides is more harmful to human health as compared to short-term exposure. Although the present study was typically focusing on sprayers in rural setting of Tanzania it applies to all exposed to pesticides including consumers of the farm produces and family members of farm workers. The data obtained in the present study will assist in new hypothesis formulation and new studies aiming to address more accurately the causality between unprotected pesticide use and adverse health effects among people at risk.

Competing Interests

We declare that, there are neither financial nor non-financial competing interests.

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