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Exposure to DDT and Hypertensive Disorders of Pregnancy Among South African Women from an Indoor Residual Spraying Region: The VHEMBE Study

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Abstract

Indoor Residual Spraying (IRS), the use of insecticides inside residences for malaria control, may cause elevated exposure to insecticides such as dichlorodiphenyl trichloroethane (DDT). Evidence suggests that DDT exposure may increase blood pressure but no study has investigated associations with hypertensive disorders of pregnancy (HDP) in an IRS area. We measured the serum concentration of DDT and its breakdown product dichlorodiphenyl trichloroethylene (DDE) at the time of delivery among 733 rural South African women participating in the Venda Health Examination of Mothers, Babies and their Environment (VHEMBE). We also collected data on HDP diagnosis through questionnaires administered to participants and medical record abstraction. We used multiple logistic regression models to examine the relation between DDT/E and HDP. *p,p'*-DDT and *p,p'*-DDE serum concentrations were associated with HDP based on self-report (OR=1.50; 95%CI=1.10, 2.03 for *p,p'*-DDT and OR=1.58; 95%CI=1.09, 2.28 for *p,p'*-DDE) and medical records (OR=1.32; 95%CI=0.99, 1.75 for *p,p'*-DDT and OR=1.47; 95%CI=1.03, 2.09 for *p,p'*-DDE). *p,p'*-DDE was also associated with gestational hypertension (OR=1.44; 95% CI=1.00, 2.07). Exposure to DDT and DDE may be associated with elevated risks of HDP in South African women residing in an area sprayed for malaria control.

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Conflict of interest
none declared.

Keywords

DDT; DDE; hypertensive disorders of pregnancy; preeclampsia; Indoor Residual Spraying; South Africa

1. Introduction¹

Banned in Western countries since the 1970s, dichlorodiphenyl trichloroethane (DDT), an organochlorine insecticide, is sprayed on the interior walls of homes to control malaria in 10 countries – 9 of which are in Africa – as part of Indoor Residual Spraying (IRS) programs (World Health Organization 2015). IRS results in elevated human exposure to DDT and dichlorodiphenyl dichloroethylene (DDE), DDT's primary breakdown product. For instance, we reported medians (interquartile range) of 736.9 (161.8–1726.7) ng/g-lipid among South African women whose homes were sprayed during pregnancy compared to 50.0 (18.6–236.9) ng/g-lipid for women living in unsprayed homes (Gaspar et al. 2017). These levels are at least 10 times higher than reported among pregnant women or women of reproductive age in the United States and Europe (Bradman et al. 1997; Centers for Disease Control and Prevention 2005; Jonsson et al. 2005). DDT and DDE are highly persistent in biological tissues and the environment, are lipid soluble and can cross the human placenta (Agency for Toxic Substances & Disease Registry 2002; Falcon et al. 2004).

Although findings have been inconsistent, some studies suggest that exposure to *p,p'*-DDT and *p,p'*-DDE (DDT/E) may be associated with hypertension in humans. In Greenland, plasma *p,p'*-DDT was associated with elevated odds of hypertension among Inuits aged 18–39 years but not in those aged 40 years and older and prenatal exposure to *p,p'*-DDT was associated with elevated risk of hypertension among California women (La Merrill et al. 2013); no association was found with *p,p'*-DDE in either age group (Valera et al. 2013b). In contrast, in another study of Inuits in Nunavik, Canada, *p,p'*-DDT plasma concentrations were associated with lower odds of hypertension while *p,p'*-DDE levels were associated with higher odds (Valera et al. 2013a). *p,p'*-DDE was also associated with increased odds of hypertension among elderly individuals in Sweden (Lind et al. 2014) but other studies based in the Canary Islands (n=428) (Henriquez-Hernandez et al. 2014), Alabama, United States (U.S.) (n=394) (Goncharov et al. 2011) and Granada, Spain (Arrebola et al. 2015) (n=297) found no association between *p,p'*-DDT or *p,p'*-DDE and blood pressure.

Despite the possible link between exposure to DDT/E and essential hypertension, only one human study has investigated associations with hypertensive disorders of pregnancy (HDP). In that study, Savitz et al. (Savitz et al. 2014) found no evidence of an association between serum concentrations of *p,p'*-DDT/E and gestational hypertension or preeclampsia among women participating in the U.S.-based Collaborative Perinatal Project conducted between 1959 and 1965 when DDT was still used in the U.S. No previous study has investigated

¹Abbreviations: BP, blood pressure; CI, confidence interval; GM, geometric mean; GSD, geometric standard deviation; HDP, hypertensive disorders of pregnancy; DDT, Dichlorodiphenyl trichloroethane; DDE, Dichlorodiphenyl dichloroethylene; DDT/E, DDT and DDE; IRS, Indoor Residual Spraying; LOD, limit of detection; LOQ, limit of quantification; OR, odds ratio; PCA, principal component analysis; SD, standard deviation; SES, socioeconomic status; VHEMBE, Venda Health Examination of Mothers, Babies and their Environment.

associations between exposure to DDT/E and HDP in IRS areas where DDT is used and populations may be more susceptible to the toxic effect of DDT than Western populations due to malnutrition, poverty and poor health.

Potential impacts of environmental exposures on HDP is of particular public health significance in Sub-Saharan Africa where HDP is the second leading cause of maternal death (Say et al. 2014). In Africa, preeclampsia complicates 2% to 17% of pregnancies (Osungbade and Ige 2011; Say et al. 2014) and, at 26%, has a case fatality rate that is orders of magnitude higher than in high-income countries (MacKay et al. 2001). The aim of the present study was thus to evaluate whether maternal serum concentrations of DDT and DDE are associated with elevated risks of HDP among women living in Limpopo Province, South Africa, an area where DDT has been used for IRS for several decades.

2. Methods

2.1 Participants

Data for these analyses were derived from the Venda Health Examination of Mothers, Babies and their Environment (VHEMBE). Methods are described in details in Gaspar et al. (2017). VHEMBE is a birth cohort study whose objective is to evaluate the relationship between exposure to IRS insecticides and maternal and child health. Women participating in the VHEMBE study were recruited from Tshilidzini Hospital in the rural Vhembe District of Limpopo Province, South Africa from August 2012 to December 2013 when they presented for delivery. Gravidas were eligible for participation if they were aged 18 years or older, spoke Tshivenda (a local language) at home, lived within 20 km of the hospital and planned to remain in the area over the following two years, had not been diagnosed with malaria during pregnancy, had contractions >5 minutes apart, and gave birth to a viable singleton. Of 920 eligible women, 152 refused enrolment, 3 did not provide a sufficient blood sample for DDT analysis, and 14 did not complete a baseline questionnaire, leaving a sample of 751. For this analysis, we excluded women who reported a diagnosis of nongestational hypertension (n=18), for a final sample of 733 women. Study participants provided written informed consent before data collection began. Committees for the Protection of Human Subjects from the University of California, Berkeley, McGill University, University of Pretoria, Limpopo Department of Health and Social Development and Tshilidzini Hospital approved all research activities.

2.2 Data collection

Data were obtained from participants using an interviewer-administered questionnaire conducted shortly after delivery. All interviews were conducted in Tshivenda by trained study staff originating from the local area and fluent in Tshivenda and English. Questionnaires were used to obtain information on HDP diagnosis, sociodemographic indicators, household assets (selected based on the Demographics and Health Survey (United States Agency International Development)), pregnancy and health history, IRS insecticide application and personal habits. Based on guidelines from Statistics South Africa, we considered the food poverty line to be at 386 South African Rands/month/person (approximately USD 30) (Statistics South Africa 2014). The questionnaire was designed in

English, translated in Tshivenda and back-translated in English by native speakers in the translated language.

Registered nurses blinded to participant's exposure abstracted hospital medical records to obtain information on diagnosis of gestational hypertension, preeclampsia, gestational age at birth, infant birth weight, and maternal HIV status.

2.3 Measurement of DDT and DDE in maternal serum

Serum samples were collected from women by venipuncture at the time of delivery and were immediately processed and stored at -80°C until shipment to the Emory University Environmental Health Laboratory where p,p' -DDT, p,p' -DDE and o,p' -DDT were measured using high-resolution gas chromatography-isotope dilution mass spectrometry (Barr et al. 2003). The limits of detection (LOD) for p,p' -DDT, p,p' -DDE and o,p' -DDT were 0.01, 0.03 and 0.01 ng/mL serum, and the limits of quantification (LOQ) were 0.03, 0.09, 0.03 and 0.03 ng/mL serum, respectively. DDT/E concentrations are expressed on a lipid basis. Total lipids were determined based on triglyceride and total cholesterol serum concentrations measured using standard enzymatic methods (Roche Chemicals, Indianapolis, IN, USA) (Phillips et al. 1989).

2.4 Outcome definitions

Primary outcomes for this study included: 1) Self-reported diagnosis of hypertension, preeclampsia or eclampsia [referred to as self-reported HDP hereafter] during the index pregnancy based on the following question: "Did a doctor or nurse ever tell you that you had high blood pressure or BP, hypertension, eclampsia, or preeclampsia?" and, if the answer was "Yes", "Was it during this pregnancy?"; and 2) Doctor diagnosis of gestational hypertension, preeclampsia or HDP (gestational hypertension or preeclampsia) based on medical records.

2.5 Statistical analysis

Analysis of variance (ANOVA) was used to examine bivariate associations between categorical variables and DDT/E while Pearson's correlations were used for continuous associations. Multiple logistic regression models were used to evaluate associations between DDT/E and gestational hypertension, preeclampsia and HDP.

Serum concentrations of DDT/E were $\log_{10}$ -transformed to reduce the influence of outliers and were categorized in quartiles. We used values generated by the instrument for serum concentrations between the LOD and the LOQ. Values below the LOD were imputed at random based on a log-normal probability distribution whose parameters were determined by maximum likelihood estimation (Lubin et al. 2004). Confounders considered for inclusion in models were identified based on Directed Acyclic Graphs (DAGs) and included the following variables (expressed as shown in Table 1 or in parentheses): maternal age at delivery (continuously); parity; socioeconomic status (SES) indicators (including maternal education, household income, poverty, number of times the mother skipped meals because there was not enough food); diabetes; smoking; alcohol consumption; and season of BP measurement (winter, spring, summer or fall). In addition, we used principal component

analysis (PCA) to develop a summary measure of household assets based on guidelines for measuring household wealth in low-income countries (Vyas and Kumaranayake 2006). Variables included whether a household member owned the following assets: home, watch, car, cellphone with internet, cellphone without internet, landline phone, computer, agricultural land, chickens or livestock, a western-style home compared to a traditional home, bicycle, motorcycle, wheelbarrow, radio, television and a bed to sleep on. We included the first component as a covariate in models. Variables were included in the final regression models if they were associated with any of the exposures or outcomes at $P<0.15$. All final models comprised the following variables: maternal age at delivery, parity, income per person, alcohol consumption during pregnancy, maternal education, the household asset summary measure and season of BP measurement. We had complete data on most covariates. Missing values ($< 0.5\%$) were imputed based on observed probability distributions. We used inverse probability weighting to account for selection bias due to missing outcome data (Hernan et al. 2004). Weights were determined by multiple logistic regression and robust (Huber-White) standard errors were computed. We also evaluated effect modification by age, body mass index, parity, HIV status and poverty by including cross-product variables in models.

We conducted sensitivity analysis to evaluate the robustness of our results. In order to ensure that the lipid correction method that we selected did not affect our results, we re-ran all analyses expressing DDT and DDE on a serum basis while including triglycerides and cholesterol as covariates in models. In addition, because body mass index could be a confounder or a variable on the causal pathway between serum DDT/E concentrations and HDP, we also conducted analyses with and without including this variable in models. We also re-ran models using alternative outcome definitions where participants were identified as cases if 1) HDP was reported by participants and was recorded in medical records ($n=42$), and 2) HDP was reported by participants or was recorded in medical records ($n=110$). Results were not substantially altered by sensitivity analyses (Supplemental Tables 1–3). We also computed Cohen's kappa to evaluate agreement between self-reported diagnosis and doctor diagnosis based on medical records. We present results with DDT and DDE concentrations expressed on a lipid basis and without controlling for body mass index.

Statistical significance was set at $P<0.05$ for main effects and $P<0.10$ for effect modification using two-sided tests. All analyses were conducted using STATA, version 13.1 (StataCorp LP, College Station, TX).

3. Results

3.1 Participant characteristics

All participants were Black/African women born in South Africa. Mean maternal age at delivery was 26.3 years ($SD=6.2$, range=18–47 years). As shown in Table 1, the majority of participants were multiparous (56%), single (52%) and had not completed high school (54%). Most participants (61%) lived below the South African food poverty level and 14% were HIV positive. Two women reported smoking, two reported using drugs and 39 (5%) consumed more than 0.5 alcoholic drinks per week during pregnancy. Fourteen percent

(n=103) of women delivered preterm (<37 weeks gestation) and 8% (n=63) of babies were born of low birth weight (<2,500 g).

3.2 Maternal DDT and DDE serum concentrations

Geometric means (GM) for maternal serum p,p' -DDT, p,p' -DDE and o,p' -DDT were 67.9 ng/g lipid [geometric standard deviation (GSD)= 6.7 ng/g lipid], 284.2 ng/g lipid (GSD= 4.9 ng/g lipid) and 8.8 ng/g lipid (GSD=4.6 ng/g lipid) with detection frequencies of 98%, 100% and 91%, respectively (Table 2). None of the maternal characteristic variables considered in this analysis were significantly associated with DDT/E serum concentrations except that women living in a home that was sprayed during pregnancy had geometric mean serum concentrations of p,p' -DDT (474.1 vs. 63.2 ng/g lipid), p,p' -DDE (1,410.2 vs. 269.0 ng/g lipid) and o,p' -DDT (33.2 vs 8.3 ng/g lipid) that were 4 to 7 times higher than women whose home was unsprayed. Serum concentrations of p,p' -DDT, p,p' -DDE and o,p' -DDT were highly correlated ($r = 0.69, 0.78$ and $0.85, p < 0.001$).

3.3 Hypertensive disorders of pregnancy

Seventy-three (10%) women reported a diagnosis of HDP during the index pregnancy. Based on medical records, 76 (12%) women were diagnosed with gestational hypertension, 15 (2%) were diagnosed with preeclampsia and 79 (13%) were diagnosed with HDP. The agreement proportion for HDP based on self-report and medical record was 90% with a kappa statistic of 0.51 ($p < 0.001$). Women with HDP were older and were more likely to be multiparous and to have less than a high school education.

3.4 Association between DDT and DDE and hypertensive disorders of pregnancy

As shown in Table 3, p,p' -DDE (OR=1.58; 95%CI=1.09, 2.28) was most strongly associated with odds of HDP based on self-report, followed by p,p' -DDT (OR=1.50; 95%CI=1.10, 2.03) and, to a lesser extent, o,p' -DDT (OR=1.37; 95%CI=0.95, 1.99). Similarly, p,p' -DDE was most strongly associated with HDP (OR=1.47; 95%CI=1.03, 2.09) and gestational hypertension (OR=1.44; 95%CI=1.00, 2.07) diagnosis based on medical records and p,p' -DDT was associated with HDP (OR=1.32; 95%CI=0.99, 1.75). Associations with preeclampsia were above the null for all three exposures but none reached statistical significance, possibly due to the small number of cases. Finally, we found no evidence of effect modification by age, body mass index, parity, HIV status or poverty. Results were similar when categorizing exposure in quartiles (Supplemental Table 4).

4. Discussion

We found associations between maternal serum concentrations of DDT/E and elevated odds of HDP diagnosis based on self-report and data abstracted from medical records in a population of South African women living in an area where IRS is conducted for malaria control. In contrast, Savitz et al. found no association between DDT/E and HDP based on BP measurements abstracted from medical records in the Collaborative Perinatal Project. This discrepancy may be partly due to differences in susceptibility between the US population studied by Savitz et al. and our African population, which experiences high rates of poverty, malnutrition and poor health. Inconsistent results may also be related to outcome

assessment. For instance, misclassification may be more likely for BP measurement than HDP diagnosis (if health care providers are more likely to omit recording data on BP than on diagnosis), which would on average drive measures of associations towards the null. Prior studies of DDT/E and hypertension, which were primarily based on measured BP, have also reported mixed results (Arrebola et al. 2015; Goncharov et al. 2011; Henriquez-Hernandez et al. 2014; Lind et al. 2014; Valera et al. 2013a; Valera et al. 2013b). Serum p,p' -DDT concentrations were associated with elevated odds of hypertension in Greenland (Valera et al. 2013b) and lower odds in Nunavik, Canada (Valera et al. 2013a) while p,p' -DDE was associated with increased odds of hypertension in Nunavik and Sweden (Lind et al. 2014; Valera et al. 2013a) but no associations were found between p,p' -DDT and/or p,p' -DDE and blood pressure in the Canary Islands, U.S. and Spain (Arrebola et al. 2015; Goncharov et al. 2011; Henriquez-Hernandez et al. 2014). Inconsistent results may be explained by a range of factors including differences in exposure levels, life stage, genetic background, and control for confounding.

Levels of DDT/E found in our study were substantially higher than in pregnant women from the 1999–2004 National Health and Nutrition Examination Survey (NHANES; median <5.1 ng/g lipid for p,p' -DDT and 131.0 ng/g lipid for p,p' -DDE) (Centers for Disease Control and Prevention 2000, 2002, 2004). It is noteworthy that the northern populations from Greenland, Nunavik and Sweden, in which associations with hypertension were found, had particularly high exposure to p,p' -DDE (GM=1,016.6 ng/g lipid; GM=6.41 µg/L; and median=290.6 ng/g lipid, respectively). These concentrations were higher than those of the VHEMBE population overall but lower than those of women whose homes were sprayed with DDT during pregnancy. However, serum concentrations did not reach those from Savitz et al. (Savitz et al. 2014) in the Collaborative Perinatal Project [median=25 µg/L or about 3,200 ng/g lipid assuming blood lipid concentrations of 7.9 g/L (Longnecker et al. 2003; Longnecker et al. 2005)] conducted when DDT was still used in the U.S. p,p' -DDT serum concentrations were higher in VHEMBE women than in prior studies of hypertension (Arrebola et al. 2015; Goncharov et al. 2011; Henriquez-Hernandez et al. 2014; Lind et al. 2014; Valera et al. 2013a; Valera et al. 2013b).

The plausibility of a causal effect of DDT on HDP and hypertension is supported by mechanistic evidence. For instance, DDT activates the renin-angiotensin system (Gascon and Brodeur 1969), a signalling pathway that may mediate the production of reactive oxygen species and play a role in hypertension (Touyz 2004). DDT and DDE have also been shown to induce oxidative stress and to cause endothelial cell dysfunction, which have been associated with preeclampsia (Bredhult et al. 2008; Perez-Maldonado et al. 2005).

This study has a few limitations. First, we measured exposure at the time of delivery and thus after outcomes occurred. However, we expect serum DDT/E concentrations measured at delivery to be representative of concentrations earlier in pregnancy given evidence from Longnecker et al. who reported that DDE serum concentrations were highly intercorrelated ($r=0.83$ to 0.92) between each trimester of pregnancy and up to 48 days postpartum among U.S. women (Longnecker et al. 1999). If DDT increases BP in the context of the metabolic syndrome (Lind et al. 2013; Uemura et al. 2009), individuals with higher concentrations of DDT would have increased fat mass, which would dilute concentrations of lipophilic

chemicals on a blood lipid basis, as discussed by Chevrier (2013) and Erkin-Cakmak et al. (Erkin-Cakmak et al. 2015). Mixed findings in the literature and in our study may thus be due in part to reverse causality, which would bias associations toward the null. In addition, statistical power may have been affected by the small number of preeclampsia cases. Outcomes were based on self-report or medical records, which may have introduced measurement error. However, because participants and nurses abstracting medical records were blinded to the research question, any misclassification should be nondifferential with respect to the outcome. This would be expected to bias estimates towards the null and thus could not explain our results. Finally, we did not measure salt consumption, which is an established risk factor for hypertension. However, salt intake is not expected to be associated with exposure to DDT/E and thus confounding should be limited.

This study has several strengths. This is the first study to investigate associations between DDT and HDP in a region where IRS insecticides are used to control malaria. In order to assess the robustness of our results, we used different data sources to identify cases of HDP including self-reported diagnosis and medical records diagnoses. Each of these has its advantages and drawbacks. Self-reported diagnosis can be most easily obtained and is thus least likely to produce missing data but may be particularly prone to outcome misclassification. However, in this study, participants and clinicians were blind to the specific hypothesis investigated and thus differential misclassification is unlikely. Diagnoses based on medical records should be most reliable but missing data and erroneous diagnoses can affect data quality. Other strengths include the detailed information that we had on potential confounders including assets (e.g., bicycle, watch, car, phone with or without internet), home, agricultural land and livestock ownership which may more adequately represent social standing in the VHEMBE population than standard variables such as education and income. Finally, we conducted sensitivity analysis to further evaluate the robustness of our results and we used inverse probability weighting to adjust for selection bias.

In summary, we present results suggesting that exposure to p,p' -DDT and p,p' -DDE may be associated with HDP in a population of African women living in an IRS area with the strongest evidence for a relation between p,p' -DDE and HDP. If replicated, these findings could have profound public health significance since HDP is associated with increased risks of pregnancy-related maternal and fetal mortality, 99% of which occurs in developing countries (Duley 2009). Gestational hypertension can lead to preeclampsia whose only established treatment is early delivery, which is related to adverse maternal and infant health outcomes (Bhutta et al. 2002). Although effective in controlling malaria, very few studies have investigated the potential adverse consequences of IRS on the health of African women. Further studies are warranted to confirm whether exposure to DDT/E is associated with HDP and other plausible health outcomes in IRS areas.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- DDT is used in 10 countries to control malaria
- Prior studies suggest associations between DDT and essential hypertension
- No study of hypertensive disorders of pregnancy in countries currently using DDT
- In this study, DDT and DDE are associated with hypertensive disorders of pregnancy
- Further studies are needed to confirm this finding

Geometric mean and geometric standard deviation of DDT and DDE serum concentrations (ng/g lipid) by maternal characteristic among VHEMBE study participants, Limpopo, South Africa, 2012–2013 (n=733).

Table 1

	n ^a	$\overline{p,p'-DDT}$		$\overline{p,p'-DDE}$		$\overline{o,p'-DDT}$		
		GM	GSD	GM	GSD	GM	GSD	
Age at delivery (years)								
18–20	178	24	65.7	8.4	331.8	5.3	9.4	4.8
21–25	232	32	69.6	6.2	261.5	5.0	8.5	4.7
26–30	157	21	73.4	5.9	316.1	4.5	8.7	4.2
≥31	166	23	63.1	6.6	244.5	4.4	8.6	4.8
Parity ^b								
0	319	44	68.9	7.6	347.4	5.3	8.9	4.7
1	200	27	66.2	5.1	238.9	4.5	8.0	4.3
≥2	214	29	68.0	7.0	247.8	4.4	9.3	4.7
Gestational age at delivery (weeks)								
<37	103	14	64.9	6.6	299.3	4.8	9.2	4.4
37–42	579	79	67.6	6.9	283.5	4.9	8.6	4.7
>42	51	7	78.5	5.0	263.1	4.6	9.2	4.2
Education								
<High School	399	54	69.8	6.9	273.8	5.0	9.0	4.9
High School	226	31	77.2	6.4	326.9	4.7	9.3	4.4
>High School	108	15	47.1	6.3	243.2	4.6	7.2	4.1
Household income ^c								
≥Poverty line	284	38	57.0	6.8	274.1	4.5	7.9	4.1
<Poverty line	446	61	76.2	6.6	292.1	5.1	9.4	4.9
Alcohol during pregnancy								
Yes	39	5	90.5	6.5	392.9	3.7	10.0	5.5
No	694	95	66.8	6.7	279.1	4.9	8.7	4.6
HIV Status								
Positive	103	14	63.1	5.9	265.6	4.3	7.7	4.4
Negative	630	86	68.7	6.8	287.4	5.0	9.0	4.6

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	$\overline{p,p'-DDT}$		$\overline{p,p'-DDE}$		$\overline{o,p'-DDT}$	
	GM	GSD	GM	GSD	GM	GSD
n^a	% ^a					
Smoking during pregnancy						
Yes	2	<1	50.9	1.6	669.2	1.3
No	731	99	68.0	6.7	283.5	4.9

Abbreviations: GM, geometric mean; GSD, geometric standard deviation.

^aFrequencies may not add to the total number of participants due to missing values. Percentages may not add to 100% due to rounding.

^bParity is determined based on the number of fetuses delivered at a gestational age of 24 weeks or more.

^cPoverty based on household income < 386 South African Rands (ZAR) per month (approximately 30 USD).

Table 2

Serum concentrations of DDT/E (ng/g lipid) in pregnant women participating in the VHEMBE study, Limpopo, South Africa, 2012–2013 (n=733).

	Detection frequency (%)	GM	GSD	Min	25 th	Median	75 th	Max
<i>p,p'</i> -DDT	98.0	67.9	6.7	<LOD	18.6	52.5	257.1	15027.6
<i>p,p'</i> -DDE	100.0	284.2	4.9	<LOD	88.7	239.0	878.1	26,301.3
<i>o,p'</i> -DDT	90.6	8.8	4.6	<LOD	3.4	7.0	22.6	2029.3

Abbreviations: Max, maximum; Min, minimum; GM, geometric mean; GSD, geometric standard deviation; 95% CI; 95% confidence interval.

Table 3

Association between log10-transformed DDT/E serum concentrations (ng/g lipid) and hypertensive disorders of pregnancy among pregnant women participating in the VHEMBE study, Limpopo, South Africa, 2012–2013.

	Total n	Cases n	Controls n	$\log_{10}$ -DDT ^a		$\log_{10}$ -DDE ^a		$\log_{10}$ -DDT ^a	
				OR	(95%CI)	OR	(95%CI)	OR	(95%CI)
<u>Self-reported diagnosis</u>									
HDP	733	73	660	1.50	(1.10, 2.03)	1.58	(1.09, 2.28)	1.37	(0.95, 1.99)
<u>Physician diagnosis</u>									
Gestational Hypertension	626	76	550	1.28	(0.95, 1.72)	1.44	(1.00, 2.07)	1.22	(0.81, 1.83)
Preeclampsia	633	15	618	1.26	(0.74, 2.16)	1.14	(0.62, 2.10)	1.48	(0.86, 2.56)
HDP	626	79	547	1.32	(0.99, 1.75)	1.47	(1.03, 2.09)	1.23	(0.83, 1.82)

Abbreviations: HDP, hypertensive disorders of pregnancy; OR, odds ratio; 95%CI, 95% Confidence Interval

^aModels adjusted for maternal age at delivery, parity, income per person, maternal education, household asset summary measure, alcohol consumption during pregnancy and season.