Agricultural pesticide exposure and perinatal mortality in central Sudan

T.E. Taha¹ & R.H. Gray²

Hospital- and community-based studies were conducted in central Sudan to investigate the association between pesticide exposure and perinatal mortality. The cases were 197 stillbirths in the hospital and 36 perinatal deaths in the community; the controls were 812 liveborn, normal-birth-weight infants in the hospital, and 1505 liveborn infants who survived for the first 7 days after birth in the community. The odds ratio (OR) of perinatal death associated with pesticide exposure was estimated using multiple logistic regression. There was a consistent and significant association between pesticide exposure and perinatal mortality in the hospital (adjusted OR = 1.9; 95% confidence interval (CI): 1.3–2.8) and the community populations (adjusted OR = 2.7; 95% CI: 1.1–6.4). The OR was significantly higher among women engaged in farming (3.6; 95% CI: 1.6–8.0), but not among women in nonfarming occupations (1.6; 95% CI: 0.8–3.3). The estimated attributable risks of perinatal death owing to pesticide exposure were 22.6% for hospital stillbirths and 15.7% for community perinatal deaths; but among women engaged in farming in the hospital population the attributable risks were substantially higher (34.5%).

Introduction

Perinatal mortality is high in developing countries, and although precise levels are difficult to gauge because of underreporting, it is estimated that there are about 7 million perinatal deaths per annum in developing countries (1). Numerous biological and social factors contribute to perinatal mortality, but with increasing industrial development and modernization of agriculture, occupational and environmental factors are becoming more important.

Pesticides comprise a wide range of compounds, including insecticides, fungicides and herbicides (2). Although such substances are used extensively in developing countries and there are numerous reports of acute toxic exposures in adults (3–5), few studies of the reproductive effects of pesticides have been conducted. One such investigation of cotton-field workers in India reported a decrease in male fertility and increased rates of spontaneous abortions, stillbirths, neonatal deaths, and birth defects among the wives of men exposed to pesticides (6). In Colombia, moderate increases in spontaneous abortion, congenital malformation, and prematurity rates have been reported among females who worked in horticulture, where a variety of pesticides were used (7).

Most studies on the reproductive effects of pesticide exposures have been carried out in developed countries. For example, two Canadian studies reported increased stillbirth rates among women employed in agricultural or horticultural work (8) and among women workers exposed to low levels of pesticides or germicides (9). Another Canadian investigation found an increased risk of stillbirths among mothers exposed to pesticides during the second trimester of pregnancy, and noted variations in stillbirth rates associated with seasonal exposure to pesticides (10). Also, in Sweden an excess of perinatal deaths has been observed among agricultural workers (11).

The Gezira Scheme in central Sudan is the largest and oldest agricultural project in the country, with around 0.8 million hectares of land under irrigation. Traditionally, cotton was the main cash crop, but recently wheat, sorghum, groundnuts, and vegetables have been introduced. Extensive aerial and ground spraying is carried out to protect these crops, and there are numerous cases of adult pesticide poisoning (12).

The current study was designed to assess the risk factors contributing to perinatal mortality and low birth weight in central Sudan, and in this article we address the association between perinatal mortality and exposure to agricultural pesticides.
Materials and methods

Hospital- and community-based studies were conducted concurrently in central Sudan. Wad Medani and Sennar, the main referral hospitals in the area, were chosen for the hospital investigation. Surveillance of all births in these hospitals was carried out and a case-control study was performed in which the cases were stillbirths (defined as birth of a dead child of birth weight >500 g) and the controls were a sample of normal liveborn infants of birth weight ≥2500 g. The study was conducted between March 1989 and June 1990.

The community study covered all six health centres located between Wad Medani and Sennar cities. These health centres represent the approximate catchment area of the two hospitals and each provides routine primary care, a senior midwife (health visitor), and antenatal and postnatal care. The health visitors also supervise village midwives who conduct home deliveries and provide antenatal care at the health centre. All 34 midwives and the health visitors who worked in the health centres participated in the investigation—a community, midwife-based, surveillance and follow-up study. A cohort of all midwife-assisted births over the period April 1989 to March 1990 was identified and followed postnatally. Perinatal deaths (i.e., stillbirths + early neonatal deaths in the first week of life) were compared with liveborn normal-birth-weight infants who survived the early neonatal period.

A trained senior nurse or a study worker collected information on sociodemographic and medical/obstetric factors, as well as on pesticide exposure by interviewing the mothers using a structured questionnaire. Anthropometric measurements of mothers and infants were made shortly after birth, and laboratory and clinical measurements were also obtained for the hospital population. The study personnel were regularly supervised by one of the investigators (T.E.T) and specially trained study coordinators. Listings of the chemicals used in the irrigation area were obtained from the Sudan Gezira Board, and potentially hazardous substances were identified by reviewing toxicological data.

Pesticide exposure was defined as a history of exposure to spraying during pregnancy, but it was not possible to determine the type of chemical, dose, or when it occurred. No antimalarial spraying was carried out in the area during the study period. In urban areas, indoor spraying of insecticides using hand pumps is common but aerosol sprays are extremely expensive and generally not available; in rural areas, most spraying is associated with agriculture. Thus, it is likely that most spraying in urban areas was of insecticides for domestic use, whereas in rural areas, agricultural spraying was the predominant exposure. Information was obtained on the type of work performed by the mother during pregnancy, paternal occupation, and place of residence. For the hospital population, a woman’s occupation was classified as “farming” if the couple resided in a rural area, the mother described her work during pregnancy as heavy (e.g., farming, carrying water or firewood), and the husband’s occupation was farming. Those mothers who did not satisfy these criteria were classified as “nonfarmers”. In the community study, all women were rural residents involved in agricultural activities.

Descriptive, bivariate, and multivariate statistical methods were used in the analysis. The crude and the adjusted odds ratios (OR) and 95% confidence intervals (CI) were estimated to determine the association between exposure to pesticides and the occurrence of stillbirths and perinatal deaths. A multiple logistic regression analysis (SAS version 5.18) was used to control for potential confounding and to appraise interactions. All variables associated (P<0.1) with stillbirths or perinatal mortality in preliminary multivariate regression models were included in the final regression analysis. The adjusted population-attributable risk percentage (i.e., the maximum proportion of the disease attributed to exposure after adjusting for the effects of possible confounding factors) was estimated from the adjusted OR and the proportion of cases in each strata of the risk factor (13).

Results

There were 197 stillbirths and 812 liveborn controls in the hospital study, and 36 perinatal deaths and 1505 liveborn normal-birth-weight controls in the community study. Table 1 shows the distribution of hospital and community cases and controls, and the unadjusted odds ratios for perinatal death associated with exposure to spraying. In both the hospital and the community populations, the mothers of the dead children reported a higher frequency of exposure to spraying during pregnancy than did the mothers of the liveborn controls. The OR for stillbirths in the hospital study (1.5) was similar to that for perinatal deaths in the community (1.6). Among the hospital population, the OR for stillbirths associated with pesticide exposure was particularly high (3.6) for women in farming occupations.

A number of other factors were also associated with stillbirths or perinatal death, including the following: place of delivery, prior reproductive loss, maternal postnatal weight, the number of antenatal care visits, use of iron supplements and vitamins during
Table 1: Distribution of hospital and community cases and controls, by exposure to spraying and occupation, central Sudan, 1989–90

<table>
<thead>
<tr>
<th>Exposure to pesticides and perinatal mortality in Sudan</th>
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<table>
<thead>
<tr>
<th></th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Odds ratio*</th>
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<tbody>
<tr>
<td><strong>Hospital</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>197 (47.2)b</td>
<td>812 (38.2)</td>
<td>1.5; 1.1–2.0c</td>
</tr>
<tr>
<td>Stratified by occupation:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Farmers</td>
<td>29 (48.0)</td>
<td>103 (20.4)</td>
<td>3.6; 1.4–9.6</td>
</tr>
<tr>
<td>Nonfarmers</td>
<td>168 (47.0)</td>
<td>709 (40.8)</td>
<td>1.3; 0.9–1.8</td>
</tr>
<tr>
<td><strong>Community</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>36 (25.0)</td>
<td>1505 (16.9)</td>
<td>1.6; 0.7–3.7</td>
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</table>

* Unadjusted.
* Figures in parentheses are the % exposed to spraying.
* Figures in italics are the 95% confidence intervals.

pregnancy, birth-to-conception interval, other illnesses, place of delivery of the last birth, delivery complications, birth defects, and infant's sex. Table 2 shows the results of the multivariate analysis after adjusting for these factors. After adjusting for potential confounders, there was a significantly increased risk of stillbirth (OR = 1.9) in the hospital population and of perinatal death in the community population (OR = 2.7). Table 2 also shows the adjusted odds ratios for the interaction of occupation and pesticide exposure in the hospital study population. Pesticide spraying was associated with a significantly increased risk among women engaged in farming (OR = 3.6), but the risk was only moderate and not statistically significant among nonfarmers (OR = 1.6). The adjusted attributable risks associated with pesticide exposure were estimated to be 22.6% for hospital stillbirths and 15.7% for community perinatal deaths. However, for the hospital population the attributable risk was estimated to be 34.5% among women engaged in agriculture compared with 10.7% for nonfarmers.

The frequency of major birth defects among the hospital population was similar among stillborn infants whose mothers reported exposure to spraying (2.2%) and those who reported no such exposure (2.5%), even after adjusting for parental occupation and place of residence.

**Discussion**

The results of the study indicate a consistent and statistically significant association between exposure to pesticides during pregnancy and increased risk of stillbirth or perinatal death (see Table 1). Stratification of the hospital population by occupation and residence showed that the risk of stillbirth was significantly higher among exposed farmers, suggesting that exposure to agricultural pesticides has adverse reproductive consequences. Also, the results of the multivariate analysis showed that the adjusted risk of stillbirth following pesticide exposure was significantly higher for farmers, while for nonfarmers it was modest and not significant (see Table 2).

Although our results do not prove that exposure to agricultural pesticides causes perinatal death, a causal association is plausible, as outlined below.

- Exposure to agricultural pesticides is common in the study population. Aerial and ground spraying of cotton and other crops (about 8 rounds per season) is carried out over a large irrigated area in central Sudan (14), and the country has the highest number of cases of pesticide intoxication reported in Africa (12).
- Other sources of insecticides cannot account for the observed association. Indoor spraying for malaria was reduced in 1988 and terminated during 1989 because of financial constraints and a change in the malaria control strategy (15, 16). Thus, insecticide exposure resulting from malaria control was infrequent during the study period.

In the study the questions on exposure did not specifically differentiate between household and agricultural spraying. However, it is unlikely that the respondents used aerosol sprays in the home since such sprays are expensive and not available in most African countries (17). The high prevalence of exposure to spraying among urban nonfarmers (41–47%) is probably attributable to other forms of domestic insecticides since we found no significant association between spraying and stillbirth for these women.

Table 2: Adjusted odds ratios and 95% confidence intervals for hospital stillbirths and community perinatal deaths associated with pesticide exposure, central Sudan, 1989–90

<table>
<thead>
<tr>
<th>Odds ratios:*</th>
<th>Hospital stillbirths</th>
<th>Community perinatal deaths</th>
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</thead>
<tbody>
<tr>
<td>Exposure to any pesticide spraying</td>
<td>1.9 (1.3–2.8)b</td>
<td>2.7 (1.1–6.4)</td>
</tr>
<tr>
<td>Spraying/farmer</td>
<td>3.6 (1.6–6.0)</td>
<td></td>
</tr>
<tr>
<td>Spraying/nonfarmer</td>
<td>1.6 (0.8–3.3)</td>
<td></td>
</tr>
<tr>
<td>No spraying/farmer</td>
<td>0.5 (0.3–1.1)</td>
<td></td>
</tr>
<tr>
<td>No spraying/nonfarmer</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted for the following variables: hospital (or community region); prior reproductive loss; maternal postnatal weight; antenatal care; use of iron and vitamins during pregnancy; birth interval; other illnesses; place of delivery of last birth; delivery complications; birth defects; and infant's sex.
* Figures in parentheses are the 95% confidence intervals.
Furthermore, the strong significant interaction between farming and pesticide exposure (Table 2) and the high attributable risk for the farmers (34.5%) suggest an exposure in the workplace rather than in the home.

After examining the list of all the agricultural pesticides used in the Gezira Scheme, we conducted a computer-aided search for the toxicological effects of 50 of the chemicals involved. Of 23 of these substances that were located on the TOXNET toxicological database, 17 compounds (organophosphates (47%), pyrethrins or pyrethrroids (24%), organochlorines (12%), carbamates or formamidines (12%) and unclassified (5%)) had fetotoxic, mutagenic, or teratogenic effects in animals or humans. These compounds are mainly used for their insecticidal, herbicidal, fungicidal, acaricidal, or molluscicidal activity (18). The present study, however, was not specific enough to identify exposure to individual substances.

In summary the strength of the association between exposure to pesticides and the occurrence of stillbirths or perinatal deaths after adjustment for other potential confounders, the consistency of the results between the hospital and the community studies, and concordance with other reports from developed (8–11) and developing countries (6, 7), suggest that the association was causal. Also, the high attributable risk estimates indicate that pesticide exposure may have substantial effects on perinatal mortality in the study population. Clearly, pregnant women should be protected from exposure to pesticides and urgent measures are needed to increase awareness about this and to use safer chemicals. Further research is also required to identify the types of pesticides that might constitute specific hazards for pregnant women and their children.

Acknowledgements
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Résumé
Exposition aux pesticides agricoles et mortalité périnatale dans le centre du Soudan

De nombreux facteurs biologiques et sociaux contribuent à élever la mortalité périnatale dans les pays en développement; toutefois, avec le développement agricole et industriel, les facteurs environnementaux commencent eux aussi à poser des problèmes particuliers. Bien que les pesticides agricoles soient eux aussi largement utilisés dans les pays en développement, l’effet de ces substances sur la reproduction humaine n’a été que peu étudié. Dans le centre du Soudan, des pulvérisations aériennes et au sol sont pratiquées à grande échelle (environ 8 fois par saison) dans la région de la Gezira, où le coton et les autres cultures couvrent environ 0,8 million d’hectares de terres. De plus, des pulvérisations d’insecticides pour lutter contre le paludisme ont été faites au fil des ans.

Afin de déterminer l’association entre la mortalité périnatale et l’exposition aux pesticides agricoles, nous avons effectué des études cas-témoins en hôpital et des études de suivi dans la communauté dans le centre du Soudan en 1989 et 1990. A l’hôpital, les cas étaient des morts-nés pesant plus de 500 g, et les témoins étaient constitués par un échantillon d’enfants nés vivants de poids de naissance normal (≥2500 g). Dans la communauté, une cohorte constituée de l’ensemble des naissances assistées par une sage-femme sur une année civile a été identifiée et suivie après la naissance. Les nourrissons décédés pendant la période périnatale (mortalités et décès néonataux précoces) ont été comparés avec les nourrissons nés vivants et de poids normal, qui ont survécu à la première période néonatale. Des enquêteurs qualifiés ont recueilli les informations sur les facteurs socio-démographiques et médicaux/obstétricaux, et les données sur l’exposition aux pesticides (antécédents d’exposition à une pulvérisation d’insecticide pendant la grossesse) au moyen d’un questionnaire structuré. Les données ont été analysées par détermination des odds ratios (OR) bruts et ajustés et des limites de confiance à 95%. Une analyse par régression logistique multiple a été utilisée pour prendre en compte les facteurs confondants éventuels et évaluer les interactions. Les risques attribuables ont été estimés à partir des odds ratios ajustés et de la proportion de cas dans chaque strate de facteur de risque.

Les résultats ont mis en évidence une association marquée entre la mortalité périnatale et l’exposition aux pesticides, aussi bien dans l’étude conduite à l’hôpital que dans l’étude en communauté. De plus, dans l’étude hospitalière, l’exposition aux pesticides était associée à un risque significativement augmenté chez les femmes employées dans l’agriculture (OR = 3,6), alors que le risque n’était que modéré et non statistiquement significatif chez les femmes ne travaillant
pas dans l'agriculture (OR = 1,6). Le risque attribuable a été estimé à 22,6% pour les mortalités en milieu hospitalier et à 15,7% pour les décès dans la communauté en période périnatale. Dans la population hospitalière, le risque attribuable était estimé à 34,5% chez les femmes travaillant dans l'agriculture contre 10,7% pour les autres.

La convergence des résultats entre les études en milieu hospitalier et en communauté, l'interaction marquée et significative entre la pratique de l'agriculture et l'exposition aux pesticides, les risques attribuables élevés chez les femmes travaillant dans l'agriculture, et l'emploi répandu des pesticides agricoles à un moment où les pulvérisations d'insecticides contre le paludisme avaient été arrêtées, indiquent une association de cause à effet entre la mortalité périnatale et l'exposition aux pesticides agricoles. Il est urgent de prendre des mesures afin d'améliorer la prise de conscience de ce problème, d'éviter que les femmes enceintes ne soient exposées aux pesticides, et d'utiliser des pesticides plus sûrs.

References