A Population-Based Prospective Cohort Study of Personal Exposure to Magnetic Fields during Pregnancy and the Risk of Miscarriage

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Abstract: To study the effect of magnetic fields on the risk of miscarriage, we conducted a population-based prospective cohort study among pregnant women within a large health maintenance organization. All women with a positive pregnancy test at less than 10 weeks of gestation and residing in the San Francisco area were contacted for participation in the study. We conducted in-person interviews to obtain information on risk factors for miscarriage and other potential confounders. All participants were also asked to wear a magnetic field-measuring meter for 24 hours and to keep a diary of their activities. Pregnancy outcomes were obtained for all participants by searching the health maintenance organization's databases, reviewing medical charts, and telephone follow-up. We used the Cox proportional hazard model for examining the magnetic field-miscarriage association. A total of 969 subjects were included in the final analyses. Although we did not observe an association between miscarriage risk and the average magnetic field level, miscarriage risk increased with an increasing level of maximum magnetic field exposure with a threshold around 16 milligauss (mG). The rate ratio (RR) associated with magnetic field exposure ≥16 mG (*vs* <16 mG) was 1.8 [95% confidence interval (CI) = 1.2–2.7]. The risk remained elevated for levels (in tertiles) of maximum magnetic field exposure ≥16 mG. The association was stronger for early miscarriages (<10 weeks of gestation) (RR = 2.2, 95% CI = 1.2–4.0) and among "susceptible" women with multiple prior fetal losses or subfertility (RR = 3.1, 95% CI = 1.3–7.7). After excluding women who indicated that their daily activity pattern during the measurements did not represent their typical daily activity during pregnancy, the association was strengthened; RR = 2.9 (95% CI = 1.6–5.3) for maximum magnetic field exposure ≥16 mG, RR = 5.7 (95% CI = 2.1–15.7) for early miscarriage, and RR = 4.0 (95% CI = 1.4–11.5) among the susceptible women. Our findings provide strong prospective evidence that prenatal maximum magnetic field exposure above a certain level (possibly around 16 mG) may be associated with miscarriage risk. This observed association is unlikely to be due to uncontrolled biases or unmeasured confounders. (EPIDEMIOLOGY 2002;13:9–20)

Key words: electromagnetic fields, miscarriage, cohort study, pregnancy.

The health effect of magnetic fields (MFs) of extremely low frequency has remained controversial despite efforts to reach consensus.[1,2] The main challenges in studying MF are (1) accurately measuring MF exposure level during the relevant time period and (2) identifying susceptible populations.

Ever since the first report of a potential effect of electromagnetic fields (EMFs) on the risk of childhood leukemia,[3] studying the health effect of EMF has mainly been focused on cancer risk.[4–9] Although the correct measurement of MF exposure should be *personal* exposure during the etiologically relevant time period, MF exposure in most studies was measured by surrogate, including wire code classification of the residence and residential spot measurement, frequently measured retrospectively.[3,5,8] Residential spot measurement does not capture all personal MF exposure at home and ignores exposure outside the residence. Wire code classification correlates poorly with actual residential MF level.[10] Imprecise measurement of MF exposure coupled with mis-

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specification of the relevant exposure period could lead to significant misclassification of MF exposure level, which, if nondifferential, would dilute any true effect. Consequently, it was not surprising that many studies failed to detect an effect of MF exposure, if one exists. More recent studies with more accurate measurement of MF exposure in the relevant time period have tended to report an association with the exposure.[7,11–16]

With rare exceptions,[17] no attempt has been made to identify a population susceptible to MF. It is conceivable that the biological effects of MF will most likely be felt among the population most vulnerable to environmental insults such as MF. If a true MF effect is difficult to detect owing to exposure misclassification, then a failure to identify susceptible populations further reduces the ability to detect an MF effect, especially if the susceptible population consists of only a small part of the study population.

The association between MF exposure and the risk of miscarriage has been studied only to a limited extent, and the examination has mostly been for exposure to video display terminals (VDTs). Because of the limited amount of MF emitted from VDTs,[18] however, VDTs are unlikely to be a major source of MF in a woman's daily life. Therefore, it would be difficult to detect an association of miscarriage with VDT use, even if one does exist.[19,20] One study with actual measurement of VDT MFs, however, indicated that when a woman was exposed to a VDT with a high MF level [a peak level >9 milligauss (mG)] during pregnancy, she had a more than 3-fold increased risk of miscarriage.[21] Another case-control study reported an association between an increased residential spot MF level obtained retrospectively and risk of miscarriage including subclinical abortion determined by measuring serum human chorionic gonadotropin level.[22] Use of electric blankets has also been associated with risk of miscarriage.[23]

We carried out a prospective cohort study to examine the association between 24-hour personal MF exposure and miscarriage. A previous study had suggested that a time-weighted average (TWA) MF exposure above 2 mG conveyed an excess risk.[24] The current study was funded by the California EMF Program to test this hypothesis. The funding authorities agreed that we were free to evaluate the association of other exposure metrics with miscarriage. Accordingly, in addition to TWA, we also examined one metric of interest to us, the maximum MF (MMF) encountered during the day.

Subjects and Methods

We conducted a population-based prospective cohort study among eligible female members of the Kaiser Permanente Medical Care Program (KPMCP) in Northern California. All KPMCP women who resided in San Francisco County and adjacent parts of San Mateo County and who had a positive pregnancy test at either the San Francisco or the South San Francisco KPMCP facility from October 1996 through October 1998 were identified through the computerized laboratory database as potential eligible subjects. A woman's second pregnancy, if any, during the study period was not eligible for the study. An invitational flyer describing the purposes and procedures of the study was distributed to every woman who submitted a urine sample for a pregnancy test. The flyer included a postage-paid and self-addressed return refusal postcard. Those women with positive tests from whom we did not receive the refusal postcard were contacted by a well-trained female interviewer to determine their eligibility for the study. All English-speaking women who indicated their intention to carry their pregnancy to term at this contact and whose gestational age at the pregnancy test was 10 complete weeks or less were eligible for the study.

We identified a total of 2,729 eligible pregnant women. Among them, 1,380 (50.6%) women initially agreed to participate in the study, of whom 1,063 (39.0%) completed an in-person interview and MF exposure measurement. The remaining subjects (11.6%) were never able to schedule the interview despite their initial agreement. The main reasons for refusing participation (1,185 subjects) were: (1) too busy/not interested/too stressful to participate (47.9%), (2) husband's objection (11.1%), (3) had miscarried already and would rather not talk about it (7.3%), (4) unwilling to wear the meter (6.2%), (5) other miscellaneous reasons (8.3%), and (6) no specific reasons given (19.0%). In addition, 164 women were not interviewed because they were too far along in their pregnancy (>15 weeks of gestation) when they were finally reached by our interviewers.

In-Person Interview

All participating women were interviewed in person by a well-trained interviewer to obtain detailed information on known risk factors for miscarriage and other adverse pregnancy outcomes, as well as potential confounders. The women were also asked about their residential and occupational exposures to MF including the use of appliances, as well as their daily activities during pregnancy.

Magnetic Field Measurements

Measurement of Personal Magnetic Field Exposure

To measure her MF exposure during pregnancy, each participating woman was asked to wear an EMDEX-II meter for 24 hours starting immediately after the in-person interview. The EMDEX-II was initiated in advance with a custom program to collect MF measurements every 10 seconds and store both broadband (40–

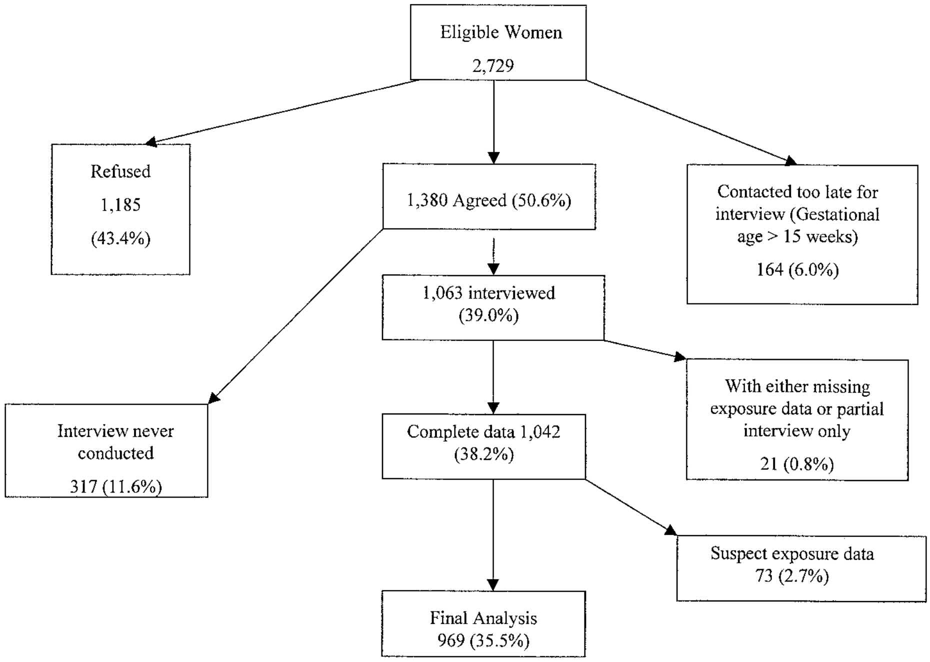

FIGURE 1. Recruitment process.

800 Hz) and harmonic (100–800 Hz) resultant MF levels. The meter was specifically programmed only to show the time of day on the display without revealing any MF exposure level so that participants would remain blinded to the MF exposure level. Subjects were also asked to keep a diary recording their activities during this period.

At the end of the measurement period, a technician from Enertech Consultants Inc (Campbell, CA), the contracting firm for conducting MF measurements, examined the data both alone and in combination with the subject's diary. The technician resolved any concerns about the data or diary with the subject at this time. The diary and a copy of the data then were forwarded to T. Dan Bracken Inc (Portland, OR), the contracting firm for performing data management on MF exposure, for further review and incorporation into the final MF database to create summary exposure measurements for analyses. After these examinations, women whose EMDEX II data did not match the activity diary or whose EMDEX II data revealed that they had failed to wear the meter (no MF recording) were excluded from the analysis (a total of 73 subjects).

To determine whether the daily activity pattern at the 24-hour measurement represented her typical day during pregnancy, we asked each participant at the end of the 24-hour measurement whether the patterns of the following activities were "fairly similar" or "quite different": home in bed, home not in bed, at work, during travel, and other activities. If a participant answered that the daily activity pattern was "quite different" for any of these five activity categories, her measurement day was considered nontypical; thus, her MF measurements on that day may not reflect her true exposure level during her pregnancy.

Residential Spot Magnetic Field Measurements

Spot measurements were taken in the subject's bedroom, the kitchen, and the most frequently occupied room that was neither a bedroom nor a kitchen. Measurements were made at the abdominal level in the center of each room as well as the location that the subject typically occupied. In addition, measurements were taken at the front entrance of the residence and at approximately 15-foot intervals proceeding clockwise around the residence. A measurement was also made at the outside location nearest the subject's bedroom.

Wire Code and External Wiring Information

The Enertech Consultants technicians performed wire coding and collected information on external wiring by producing an aerial sketch of the residence and all overhead electric system lines within 150 feet of the residence. This information was used to determine the Wertheimer-Leeper wire-code categories, which were classified as underground, very low-current configuration, ordinary low-current configuration, ordinary high-current configuration, and very high-current configuration.[3,10]

Pregnancy Outcomes

The pregnancy outcomes for all participants were ascertained through one of the following methods: linking various automated KPMCP databases, reviewing medical charts, and telephoning those whose outcomes could not be identified through the previous two methods. Among 1,063 women who participated in the study, pregnancy outcomes for 1,058 (99.5%) participants were identified. Although the final outcomes were unknown for the remaining five subjects because of their moving out of the area, they were included in the final analysis and their pregnancy was censored at the gestational age at which they were known to have remained pregnant (all beyond 20 weeks of gestation). After excluding 21 additional women with missing data on personal exposure information or with incomplete interviews, 969 subjects were left in the final analysis. Figure 1 summarizes the recruitment and participation of the study.

Because the MF exposure was measured after the interview, neither interviewers nor participants knew their MF exposure level at the time of interview. In most cases, they were both also blinded to participants' pregnancy outcomes at the interview. Nevertheless, because our study recruited participants at an early gestational age (median gestational age at entry was 40 days) when miscarriage occurs at a higher frequency, 97 participants had already had a miscarriage at the time of interview. Of them, 78 had a miscarriage before the initial contact and the remaining 19 had a miscarriage after having given their consent to participate in the study but before their interview. They were included in the study because they resided in the same residence when the miscarriage occurred as well as meeting other eligibility criteria. Nonetheless, these women remained unaware of their MF exposure level.

Statistical Analysis

We used the Cox proportional hazards model to examine the miscarriage risk associated with MF exposure during pregnancy while controlling for potential confounders and taking into account different gestational ages at entry. A woman was considered at risk of miscarriage as soon as she had a positive pregnancy test (entry time). Gestational age in days was used as the time variable. The woman continued to be considered at risk until either she had a miscarriage or was censored. Women who had other pregnancy outcomes including ectopic pregnancy or induced abortion (3.6%) were censored at the time when those outcomes occurred. Women who remained pregnant beyond 20 weeks of gestational age (80%) were censored at 20 weeks of gestation because by definition, no miscarriage occurs after 20 weeks of gestation.

To take into account the entry at various gestational ages, the time variable (gestational age) with left-truncation was used in the proportional hazards model.[25,26] The association between MF exposure during pregnancy and miscarriage risk was evaluated at any specific gestational age only among those women who were pregnant

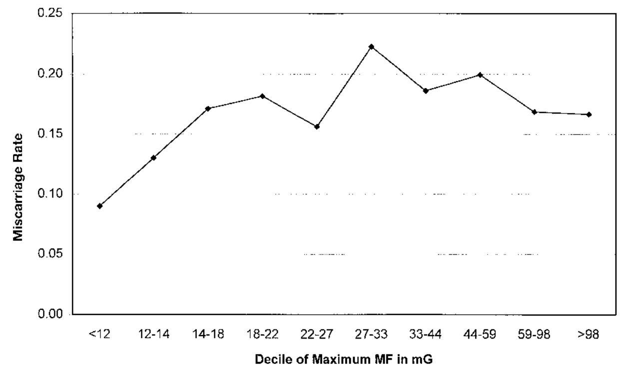

FIGURE 2. Miscarriage rate by maximum magnetic field (MF) exposure.

and had entered into the study at that time. Using the left-truncation of the time variable to reflect participants' actual contribution of their person-time to the risk assessment in the Cox proportional hazards model allowed control of any potential biases caused by the association of gestational age at entry with MF exposure and miscarriage risk. The potential confounders included in the Cox proportional hazards model were based on the known or potential risk factors for miscarriage as well as on common sociodemographic variables.

Because the mechanism of the potential effect of MF during pregnancy and the risk of miscarriage was not clear, we decided to examine the effect of the MMF level exposed for a potential threshold effect, in addition to the effect of average dose (TWA). It seemed more plausible to us that MF exposure has a threshold below which any exposure is biologically irrelevant. Thus, we postulated that MMF is a better measure for detecting the MF biological effect than TWA which, combining MF doses at all levels, is a diluted and insensitive measure.

Results

As required by the contract, we first evaluated the risk of miscarriage associated with a 24-hour TWA MF exposure $\geq$3 mG. The cutpoint of 3 mG had been chosen by the California EMF program to improve power by assuming a shallow linear dose response and by examining the exposure distribution of the cohort without knowing the case status. The rate ratio (RR) associated with TWA $\geq$3 mG was 1.2 with 95% confidence interval (CI) of 0.7–2.2. Thus, using the TWA metric failed to confirm the original findings that prompted this study.

To evaluate a potential threshold effect of MF exposure, we first examined the relation between MMF level in deciles and the risk of miscarriage. Figure 2 shows that a woman's MMF level during the 24-hour measurement period appeared to be associated with an increased rate of miscarriage, starting around 12–18 mG. The rate remained elevated with increasing MMF exposure level. Therefore, we chose 16 mG as the cutoff for all subsequent analyses because it was also the cutoff for the first quartile. The cutoff was also chosen for practical reasons because, before the data collection, we had selected several exposure levels for which other parameters of exposure dose (for example, total sum of MF, duration, and number of times above the specifically selected level) were constructed. Between 10 and 20 mG, 16 mG was the only such cutoff point that was preselected. Therefore, by choosing 16 mG, we would be able to examine other parameters of exposure.

Table 1 presents the characteristics of the exposed (MMF ≥16 mG) and unexposed (MMF <16 mG) subjects. Overall, there was little difference between the two cohorts in demographic characteristics, potential risk factors for miscarriage, reproductive history, and gestational age at entry to the study. The exposed women (MMF ≥16 mG) were more likely to have been employed before conception, to have had fever during pregnancy, and to have drunk tapwater, but they were less likely to have had a history of subfertility defined as failure in conceiving after having had regular intercourse without contraception for more than 12 months.

A few known risk factors for miscarriage, including a lack of nausea and vomiting, vaginal bleeding, maternal age ≥35 years, and prenatal smoking, were also associated with risk of miscarriage in our study population.

Prenatal exposure to MMF ≥16 mG was associated with an 80% increased risk of miscarriage. This observed association was robust against potential confounders, for the estimate barely changed after adjustment for about 30 known risk factors for miscarriage or potential confounders listed in Table 1; crude RR = 1.81 *vs* adjusted RR (aRR) = 1.80. Using total sum of MF amount ≥16 mG as a measure of dose above the threshold (taking into account both MF level and duration above the threshold), the risk of miscarriage remained elevated for higher doses of MF exposure (Table 2). Using other dose parameters including MMF in quartiles, and duration or number of times above the threshold (≥16 mG), showed a similar relation.

To determine whether the exposure to MMF ≥16 mG was simply a marker for certain activities, we examined the location of the exposure. About half of the exposed women were exposed to MMF ≥16 mG from multiple locations/activities. Among the single location of the exposure, sleeping in bed, which likely encompassed a relatively large percentage of the 24-hour measurement period, only contributed less than 1% of MMF exposure ≥16 mG. On the other hand, travel, which likely covered a relatively short time period, conveyed about 14% of the MMF exposure. The risk of miscarriage associated with MMF ≥16 mG did not vary much by the location/activity of the exposure; the risk of miscarriage was 17.7% for those who were exposed from multiple locations, 18.1% for those who were exposed only from the period at home but not in bed, 18.8% for those who were exposed only from workplace, 19.4% for those who were exposed only during travel, and 20.6% for those who were exposed from other locations/activity periods.

To evaluate whether fetuses at an early gestational age are more susceptible to MMF exposure, we examined the association separately for fetal loss before and after 10 weeks of gestation. Table 3 shows that the risk of miscarriage associated with MMF was higher for fetal loss before 10 weeks of gestation (aRR = 2.2, 95% CI = 1.2–4.0). If a fetus had survived to 10 weeks or more, the association was noticeably reduced (aRR = 1.4, 95% CI = 0.8–2.5).

To examine whether the effect of prenatal MMF exposure was greater for women who might be more susceptible to environmental insults, we restricted analyses to women who had a history of either multiple miscarriages (2 or more) or subfertility. Table 4 shows that the association of MMF with miscarriage was stronger in this group of women than in the overall population; aRR = 3.1 (95% CI = 1.3–7.7) for the exposure MMF ≥16 mG and aRR = 4.7 (95% CI = 1.4–15.9) for the exposure before 10 weeks of gestation.

To examine further the effect of the misclassified MF exposure measurement on the association, we stratified our participants by whether their activity patterns at the measurement day represented their typical daily activity patterns during pregnancy. Presumably an MF measurement obtained on a nontypical day was less likely to represent the overall MF exposure during pregnancy, resulting in more misclassification of the true MF exposure level, than an MF measurement obtained on a typical day. Table 5 shows that the association was strengthened among women whose MMF measurement was obtained during a typical day (aRR = 2.9; 95% CI = 1.6–5.3), whereas the association disappeared among women whose MMF measurements were obtained on a nontypical day (aRR = 0.9; 95% CI = 0.5–1.8). Compared with Tables 3 and 4, Table 6 also shows that after excluding the subjects with any aspect of their day characterized as nontypical, a stronger association with risk of miscarriage was consistently observed under various examinations.

Spot measurements did not show a consistent pattern of an association between increased exposure level (in quartiles) and the rate of miscarriage. In our study, the residential wire-code category was not associated with either MMF or risk of miscarriage (the results can be obtained upon request).

TABLE 1. Characteristics of Study Population by Daily Maximum Magnetic Field (MMF) Exposure Level (<16 mG or ≥16 mG)

Characteristic	Total (N = 969)	MMF <16 mG (N = 252) %		MMF ≥16 mG (N = 717) %	
		N	%	N	%
Maternal age (years)					
<20	28	7	2.8	21	2.9
20–24	107	29	11.5	78	10.9
25–29	266	69	27.4	197	27.5
30–34	327	85	33.7	242	33.8
≥35	241	62	24.6	179	25.0
Race					
White	372	89	35.3	283	39.8
Black	70	22	8.7	48	6.7
Hispanic	204	54	21.4	150	20.1
Asian or Pacific Islander	265	73	29.0	192	27.0
Other	53	14	5.6	39	5.5
Education					
<High school diploma	44	12	4.8	32	4.5
High school diploma or GED	181	51	20.2	130	18.2
Trade school/some college	311	78	31.0	233	32.5
College degree	278	72	28.6	206	28.8
Graduate school	154	39	15.5	115	16.1
Household income					
<$20,000	86	15	6.4	72	10.5
$20,000–$29,000	99	25	10.6	75	11.0
$30,000–$39,000	140	40	17.0	100	14.6
$40,000–$49,000	240	67	28.5	175	25.6
≥$50,000	348	88	37.5	263	38.4
Marital status					
Single	86	17	6.8	69	9.6
Partner	102	22	8.8	80	11.2
Married	779	212	84.5	567	79.2
Born in United States					
Yes	541	136	54.0	405	56.5
No	428	116	46.0	312	43.5
Worked in last year					
Yes	839	207	82.1	632	88.3
No	129	45	17.9	84	11.7
Smoked since LMP					
Yes	96	20	7.9	76	10.6
No	873	232	92.1	641	89.4
People smoke in house					
Yes	82	20	7.9	62	8.7
No	887	232	92.1	655	91.4
Coffee intake since LMP					
0 cups/day	662	180	71.4	482	67.2
0–1	251	58	23.0	193	26.9
>1	56	14	5.6	42	5.9
Alcohol use since LMP					
Yes	408	97	38.5	311	43.4
No	561	155	61.5	406	56.6
Drug use since LMP					
Yes	51	11	4.4	40	5.6
No	918	241	95.6	677	94.4
No. of previous pregnancies					
0	262	62	24.6	200	27.9
1	284	82	32.5	202	28.2
2	175	44	17.5	131	18.3
≥3	248	64	25.4	183	25.7
Previous miscarriage					
0	771	201	79.8	570	79.5
1	147	37	14.7	110	15.3
≥2	51	14	5.6	37	5.2
Previous induced abortion					
0	627	165	65.5	462	64.5
1	201	55	21.8	147	20.5
2	97	22	8.7	75	10.5
≥3	41	10	4.0	32	4.5
History of subfertility*					
Yes	203	64	25.6	139	19.6
No	755	186	74.4	569	80.4
Vaginal bleeding since LMP					
Yes	192	51	20.4	141	19.7
No	777	201	79.8	576	80.3
Urinary tract infection since LMP					
Yes	44	13	5.2	31	4.3
No	923	238	94.8	685	95.7

* Defined as failure in conceiving after having had regular intercourse without contraception for more than 12 months.

TABLE 1. — *Continued*

Characteristic	Total (N = 969)	MMF <16 mG (N = 252) %		MMF ≥16 mG (N = 717) %	
		N	%	N	%
Fever since LMP					
Yes	55	9	3.6	46	6.5
No	906	242	96.4	664	93.5
Flu or cold since LMP					
Yes	199	43	17.1	156	21.8
No	770	209	82.9	561	78.2
Strenuous exercise					
Yes	132	32	12.7	100	14.0
No	837	220	87.3	617	86.1
Carry loads >10 lb					
Yes	474	115	47.3	359	52.6
No	452	128	52.7	324	47.4
Used Jacuzzi since LMP					
Yes	95	19	7.5	76	10.6
No	872	233	92.5	639	89.4
X-ray since LMP					
Yes	79	20	8.0	59	8.3
No	886	231	92.0	655	91.7
Drinks tapwater					
Yes	719	166	65.9	553	77.1
No	250	86	34.1	164	22.9
Solvent use					
Yes	602	152	61.0	450	63.1
No	360	97	39.0	263	36.9
Vitamin use					
Yes	708	177	70.2	531	74.1
No	261	75	29.8	186	25.9
Diabetes mellitus					
Yes	24	7	2.8	17	2.4
No	944	245	97.2	699	97.6
Gestational age at study entry					
0–48 days	696	189	75.0	507	70.7
49–69 days	218	50	19.8	168	23.4
70–140 days	55	13	5.2	42	5.9

LMP = last menstrual period.

Discussion

Several potential limitations need to be kept in mind when one interprets the results of this study. First, our information on personal MF exposure was based on 24-hour measurement during the index pregnancy. When compared with many other studies that measured current MF exposure to reflect past MF exposure, one of the strengths of this study was that we measured MF exposure during the relevant period and used personal measurement to capture MF exposure from all sources encountered by a woman. The single 24-hour measurement, however, may not be representative of the MF exposure level during the entire relevant gestational period, resulting in misclassification of the MF exposure level. Because any misclassification of the MF exposure was unlikely to be associated with the risk of miscarriage and therefore nondifferential, it would probably have resulted in attenuation of the observed association. Nonetheless, we decided to examine further the factors that may influence this exposure misclassification.

TABLE 2. Daily Maximum Magnetic Field Exposure during Pregnancy and the Relative Risk (RR) of Miscarriage

Daily Exposure	Miscarriage Yes (N = 159)		Miscarriage No (N = 810)		RR*	95% CI
	N	%	N	%		
Maximum magnetic field						
<16 mG†	27	10.7	225	89.3	1.0	
≥16 mG	132	18.4	585	81.6	1.8	1.2–2.7
Total sum of exposure over 16 mG in tertiles						
160–1,079 mG-seconds	41	17.5	194	82.6	1.7	1.1–2.8
1,080–4,759 mG-seconds	43	18.1	195	81.9	1.8	1.1–2.9
≥4,760 mG-seconds	48	19.7	196	80.3	2.0	1.2–3.1

* Adjusted for previous miscarriage, education, maternal age, gravidity, race, and smoking since last menstrual period.
† Reference category.

TABLE 3. Daily Maximum Magnetic Field Exposure during Pregnancy and the Relative Risk (RR) of Miscarriage by Gestational Age

Gestational Age at Miscarriage	Miscarriage N	%	Person-Days*	RR†	95% CI
0–9 weeks					
<16 mG	13	0.21	6,347		
≥16 mG	81	0.48	16,963	2.2	1.2–4.0
≥10 weeks					
<16 mG	14	0.09	15,109		
≥16 mG	51	0.13	39,644	1.4	0.8–2.5

* Cumulative days at risk of miscarriage.
† Adjusted for previous miscarriage, education, maternal age, gravidity, race, and smoking since last menstrual period.

The potential misclassification of MF exposure was likely to be influenced by two factors: temporal variation in MF level and daily activity pattern. Few studies have evaluated the temporal variation of MF exposure level. One such study used repeated measurements over 12–26 months and concluded that MF level is relatively stable over the study period and that MF measurement on a single visit is a good indicator of average personal exposure levels over time, although the temporal stability of the MMF metric was not specifically examined.[10]

To examine the potential influence of a change of activity patterns on our results, we stratified the analysis of the effect on women depending on whether the measurement day was a typical day during this pregnancy. If MMF exposure is truly associated with the risk of miscarriage, one would expect the association to be stronger among women whose measurement day reflected their typical day during pregnancy. Table 5 shows that the MMF association was indeed greater among women whose MMF measurement likely reflected their true exposure during pregnancy (aRR = 2.9; 95% CI = 1.6–5.3), whereas there was no MMF association observed among women whose MMF measurements were not likely to have reflected their true exposure during pregnancy (aRR = 0.9; 95% CI = 0.5–1.8). After excluding women whose MF measurement was obtained on a nontypical day, various other measures also indicated a stronger association (Table 6). This observation provides further evidence that prenatal MMF exposure may be genuinely related to the risk of miscarriage.

Although the overall participation rate (39%) was low, this was a prospective cohort study and MMF exposure level was largely unknown to the general public. Thus, the low participation rate was unlikely to be associated with MMF exposure. In addition, although we do not know the MMF level for nonparticipants, our data records revealed that the rate of miscarriage among nonparticipants was 17.2%, compared with 16.4% among participants (Table 2), indicating comparability between participants and nonparticipants with regard to

TABLE 4. Daily Maximum Magnetic Field Exposure during Pregnancy and the Relative Risk of Miscarriage among Susceptible Populations: Women with a History of Subfertility and/or Multiple Miscarriages

Daily Exposure	Miscarriage Yes (N = 41) N	%	No (N = 198) N	%	RR*	95% CI
Maximum magnetic field						
<16 mG†	6	8.0	69	92.0	1.0	
≥16 mG	35	21.3	129	78.7	3.1	1.3–7.7
Total sum of exposure over 16 mG						
160–1,079 mG-seconds	7	14.0	43	86.0	2.3	0.7–7.2
1,080–4,759 mG-seconds	15	26.8	41	73.2	3.7	1.4–10.2
≥4,760 mG-seconds	13	22.4	45	77.6	3.3	1.2–9.2
Gestational age at miscarriage				Person-Days‡		
0–9 weeks						
<16 mG	3	0.17		1,772		
≥16 mG	27	0.77		3,503	4.7	1.4–16.0
≥10 weeks						
<16 mG	3	0.07		4,461		
≥16 mG	8	0.09		8,476	1.6	0.4–5.9

* Adjusted for previous miscarriage, education, maternal age, gravidity, race, and smoking since last menstrual period.
† Reference category.
‡ Cumulative days at risk of miscarriage.

TABLE 5. Daily Maximum Magnetic Field Exposure during Pregnancy and the Relative Risk (RR) of Miscarriage by Women Whose Daily Activities at Measurement Were and Were Not Their Typical Daily Activities during Pregnancy

	Miscarriage					
	Yes (N = 159)		No (N = 810)			
Daily Activity Pattern at Measurement	N	%	N	%	RR*	95% CI
Typical						
<16 mG†	13	8.2	146	91.8	1.0	
≥16 mG	95	20.5	368	79.5	2.9	1.6–5.3
Not typical						
<16 mG†	14	15.1	79	84.9	1.0	
≥16 mG	37	14.6	217	85.4	0.9	0.5–1.8

* Adjusted for previous miscarriage, education, maternal age, gravidity, race, and smoking since last menstrual period.
† Reference category.

their risk of miscarriage. Because we recruited women at an early gestational age (median gestational age of 40 days), 78 subjects had already had a miscarriage (49% of all miscarriage cases) at the time of initial contact for their participation. They were included in the study because measurements taken soon after miscarriage (median interval of 22 days) were considered still representative of their MMF exposure level before miscarriage. Separate analyses stratifying miscarriage cases depending on whether their measurements were taken before or after their miscarriage showed essentially the same results for both types of cases; for miscarriage <10 weeks of gestation, aRR = 5.6 (95% CI = 0.7–42.4) and 6.1 (95% CI = 1.9–20) for cases measured before and after miscarriage, respectively; for miscarriage ≥10 weeks, aRR = 1.7 (95% CI = 0.7–3.9) and 1.6 (95% CI = 0.3–7.6), respectively.

Owing to the limited studies of the MF effect on the risk of miscarriage,[18–23,27] a comparison of our results with the literature may be difficult. Nevertheless, examining the literature of the epidemiologic studies of the MF effect on other health outcomes, especially childhood leukemia, reveals that the inconsistency of results from previous studies might be attributed to a lack of adequate

TABLE 6. Various Measures of the Amount of Daily Magnetic Field Exposure during Pregnancy and the Relative Risk of Miscarriage among Women Whose Daily Activities at Measurement Were Their Typical Daily Activities during Pregnancy

	Miscarriage					
	Yes (N = 108)		No (N = 514)			
Exposure on Typical Day	N	%	N	%	RR*	95% CI
Dose-response relationship						
Maximum magnetic field <16 mG‡	13	8.2	146	91.8	1.0	
Total sum of exposure over 16 mG in tertiles						
160–1,079 mG-seconds	32	21.2	119	78.8	2.9	1.5–5.6
1,080–4,759 mG-seconds	32	20.3	126	79.7	2.9	1.5–5.7
≥4,760 mG-seconds	31	20.1	123	79.9	3.0	1.5–5.7
Effect on early or late miscarriage						
Gestational age at miscarriage			Person-Days†			
0–9 weeks						
<16 mG	4	0.10	4,030		1.0	
≥16 mG	59	0.54	11,016		5.7	2.1–15.7
≥10 weeks						
<16 mG	9	0.09	9,892		1.0	
≥16 mG	36	0.14	25,265		1.7	0.8–3.6
	Among Susceptible Population					
	Yes (N = 29; 18.1%)		No (N = 131; 81.9%)			
	N	%	N	%		
Maximum magnetic field						
<16 mG‡	5	9.1	50	90.9	1.0	
≥16 mG	24	22.9	81	77.1	4.0	1.4–11.5

* Adjusted for previous miscarriage, education, maternal age, gravidity, race, and smoking since last menstrual period.
† Cumulative days at risk of miscarriage.
‡ Reference.

exposure measurement and a failure to identify a susceptible population. Most previous studies were case-control in design and the MF exposure was often measured retrospectively, using the exposure level many years after the relevant time period to represent the actual MF level of interest in the past. Many studies only used indirect measurements of MF level such as wire code configuration. Although more recent studies have attempted direct measurements, frequently only residential spot measurements were obtained to represent a participant's overall personal MF exposure level. Residential spot measurements do not necessarily capture residential exposure, let alone overall personal exposure from all sources. All of these may compromise MF measurements and could lead to misclassification of MF exposure level (for both cases and controls), which would tend to mask an underlying MF effect. More recent studies that captured personal MF exposure and measured MF exposure closer to the relevant time period seem more likely to demonstrate an association between MF exposure and health outcomes such as childhood leukemia.[11,12,14,16]

Our study was prospective in design and measured MF exposure level at, or close to, the relevant time of interest. We used personal measurement that captured MF exposure from all sources encountered by a woman. Therefore, the MF exposure level obtained in our study better reflected the true MF exposure level in the time period of interest than most previous studies of the MF effect, thus providing a better chance to detect the adverse MF effect. Our study also demonstrated that if we stratified our analyses by whether the daily activity pattern at measurement reflected a participant's typical pattern during pregnancy, the associations with various measurements of MMF exposure were strengthened among women whose daily activity pattern at measurement was typical (Tables 5 and 6). At the same time, no association could be detected among those whose daily activity pattern at measurement was not their typical pattern during pregnancy and, thus, less likely to reflect their true MF exposure during pregnancy. This observation suggests that the lack of appropriate measurement of MF exposure during the appropriate time period may reduce the ability to detect an MF effect and may have contributed to the absence of an association in other studies.

A second factor that may be important in detecting an MF effect is the identification of a susceptible population that includes sensitive endpoints, susceptible time periods, and vulnerable populations. So far, few studies have focused on this issue.[17] Our study examined the MF effect on early and late miscarriage (<10 *vs* ≥ 10 weeks of gestation), which may be different in their sensitivity to MF exposure. Second, we evaluated the MF effect among those with a history of multiple miscarriages or subfertility, a population that suggested an underlying reproductive difficulty, and thus perhaps a high susceptibility to environmental insults. Our results suggest that MF exposure was more strongly related to early miscarriage (Tables 3 and 6) and demonstrated a stronger association with the risk of miscarriage among the susceptible population (Tables 4 and 6). It is conceivable that an embryo or fetus at early gestational age is much more sensitive to environmental insults. One of the reasons why a previously reported Finnish study was able to detect an MF association despite their crude MF exposure assessment (retrospectively obtained spot measurement) may have been that their endpoint was very early miscarriage including subclinical miscarriage.[22] Using this endpoint may have allowed the detection of a greater EMF effect owing to the increased susceptibility of embryos/fetuses at an early gestational age. Therefore, an association was detected despite the misclassified MF exposure due to the crude MF measurement. A recent study of MF and childhood leukemia also reported that the association was greater among young children (<6 years of age).[12] A higher risk among young children seems plausible if one considers the vulnerability of early childhood development and its relation to possible fetal exposure during pregnancy. Therefore, a greater ability to identify a susceptible population could enhance ability to detect an MF effect.

This population-based cohort study with prospectively measured MF exposure level revealed an increased risk of miscarriage associated with an MMF exposure level ≥ 16 mG. This association appeared to have a threshold around 16 mG and persisted regardless of the locations/activities of MMF exposure. Prenatal MMF exposure was more strongly associated with early miscarriage (<10 weeks of gestation) when embryos or fetuses are likely much more sensitive to environmental insults, and among women who may be more susceptible to environmental exposures. The association was much stronger when women whose 24-hour MF measurements may not reflect their true prenatal MF exposure were excluded. These biologically coherent observations, all based on *a priori* hypotheses, provide evidence that prenatal MF exposure above a certain level (possibly around 16 mG) may increase risk of miscarriage.

Our study did not have information on the exact sources of measured MMF ≥ 16 mG. Fields of such magnitude can be found near electric appliances (for example, microwave ovens and fluorescent desk lamps); very close to devices with electrical motors (for example, hair dryers, can openers, and fans), electric equipment in the work place, and electrically powered transit systems; and under or above certain types of power lines.

The robustness of the association between MMF and miscarriage risk against potential confounders was supported by evidence that despite adjustment for more than 30 variables of known or suspected risk factors for miscarriage, the estimates were barely altered. Moreover, prompted by the findings in this study, Lee *et al*[24] reanalyzed the data from the study in which the findings related to TWA exposure led to funding the current study and confirmed our observed association between MMF and risk of miscarriage.

The MMF exposure level in our study population was comparable with that found in a nationwide survey[28] and our study population was racially/ethnically and socioeconomically diverse.

Although the potential mechanisms of a possible MMF effect on the risk of miscarriage are not currently well understood, early fetuses are known to be sensitive to environmental insults. A disruption of early fetal development at the cellular or molecular level by external MFs could conceivably result in fetal death. Despite the lack of clear understanding of the underlying mechanisms, these findings raise the question of a possible effect of MMF on early fetal loss.

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