

An Assessment of Fertility in Boron-Exposed Workers in Turkey: An Epidemiological Approach

TÜRKİYE DE BOR İŞÇİLERİNDE FERTİLİTENİN DEĞERLENDİRİLMESİ: EPİDEMİYOLOJİK YAKLAŞIM

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Summary

Our knowledge is too limited in human reproductive data related with boron exposure. There are only a few studies reporting reduced sexual function in men occupationally exposed to boron. Some other studies, revealed that occupational or environmental exposures to inorganic borates did not lead to a reduction in birth rate. Data, about boric acid's developmental toxicities on rats, mouses and rabbits are already available. Although not significant, some studies have shown that there has been a change in sex ratios of occupationally exposed populations (in favor of female offsprings).

Since Turkey is one of the countries which has large borate deposits and plants, the conduction of the study in this area is important. The purpose of this study was to investigate borates; reproductive effects, developmental effects, and effects on the sex ratio on environmentally and occupationally exposed male workers' families in a cross-sectional design.

Study regions were planned as three areas in Turkey where Region I was Bigadiç (Balıkesir), Region II was Emet-Hisarçık (Kütahya), Region III was Kırka (Eskişehir). 850 married-male workers from these plants were chosen by random sampling method but the number of workers who were contacted were 799. Data collection was made by personal interviews of workers at their working places. For data analysis and statistics SPSS for Windows package and Chi-Square, Student's t test were used.

Infertility rates were 1.2% among 328 borate workers from Region I, 1.1% among 298 workers from Region II and 4.1% among 173 workers from Region III. Total infertility rate was 1.8% for all of the workers. These rates were similar to the results of studies made in the same region and in other parts of Turkey. Total male/female ratio was found to be 1.12, so no increase in the number of female offsprings could be found when

Özet

İnsanlarda bor maruziyeti ile ilişkili reproduktif veriler son derece kısıtlıdır. Birkaç çalışmada işyerinde bor maruziyeti olan erkeklerde cinsel fonksiyonların azaldığı belirtilmiştir. Diğer bazı çalışmalarda ise işyeri ortamı ve çevreden inorganik boratlara maruz kalınmasının doğum oranlarında bir azalma yapmadığı ortaya konmuştur. Rat, fare ve tavşan çalışmalarında borik asitin gelişim üzerinde olumsuz etkileri gösterilmiştir. Bazı çalışmalarda da istatistiksel anlamlılık olmamakla birlikte işyeri maruziyeti olanlarda doğumda cinsiyet oranının değiştiği ve kız çocuk doğma oranının arttığı iddia edilmiştir.

Türkiye geniş bor yatakları ve işletmeleri bulunan bir ülke olduğu için bu bölgede bir araştırma yapmak önemli bulunmuştur. Bu çalışmanın amacı çevresel ve işyeri bor maruziyeti olan erkek işçilerin ailelerinde borun üreme, gelişim ve cinsiyet oranı üzerine etkilerinin kesitsel olarak incelenmesidir.

Çalışma bölgesi Türkiye'deki 3 bölge olup, Bigadiç, (Balıkesir) 1.Bölge, Emet-Hisarçık (Kütahya) 2.Bölge ve Kırka (Eskişehir) 3.Bölge olarak alınmıştır. Buradaki işletmelerden 850 evli erkek işçi rasgele örnekleme ile belirlenmiş, bunların 799'una ulaşılabilmektedir. Veri toplama, işyerlerinde ve yüz yüze görüşme yöntemi ile yapılmıştır. Veri analizi ve istatistikler için SPSS for Windows paket programı ile Ki-kare ve student's t-testi kullanılmıştır, infertilite oranları 1.Bölge'de 328 işçi arasında %1.2, 2.Bölge'de 298 işçi'de %1.1 ve 3.Bölge'de 173 işçi'de %4.1 oranında bulunmuştur. Bu oranlar aynı bölgede ve Türkiye'nin diğer bölgelerinde yapılmış çalışmalarla benzerdir. Tüm işçilerde toplam infertilite oranı %1.8'dir. Toplam grup da erkek/kız oranı 1.2 bulunmuş olup, daha önceki yayınlarla kıyaslandığında doğumda kız çocuk oranında artış bulunmamıştır. Olası gelişimsel etkileri ölçmek için kullanılan parametrelerde anlamlı bir değişiklik saptanmamıştır. Ölü doğum, düşük, prematür veya düşük doğum ağırlıklı bebek olması ve bebek ölüm oranları ülkenin diğer kısımlarından çok yüksek değildir. Üretimde çalışan işçilerle, büroda çalışan işçiler arasında infertilite oranı, cinsiyet oranı ve olası

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compared with previously reported data. No significant influence was observed in parameters used to define possible developmental effects. Stillbirths, abortions, prematurities or having low birth weights and early deaths of offsprings were not more than the ones found in any part of the country. There were no differences in infertility rates, sex ratios and possible developmental effects between the production workers and office workers.

As a conclusion, the level of boron that people from the three regions were exposed to seems not to affect the reproductive characteristics investigated.

Key Words: Fertility, Boron, Workers

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Animal studies confirm that exposure to borax in high levels effects fertility in different parameters such as changes in testes and sperms or in higher doses, atrophy of the testicular tubules (1-5).

Our knowledge is limited on human reproductive data related with boron exposure. Few studies have reported reduced sexual function in men exposed occupationally to boron (6,7). In some other studies, authors have concluded that occupational or environmental exposures to inorganic borates did not lead to a reduction in birth rate (8,9). For developmental toxicity data on boric acid were available from rat, mouse and rabbit studies (10,11).

Although it was not significant, in some studies there was an excess of the percentage of female offsprings and differences in sex ratio for occupationally exposed populations (8).

Since Turkey is one of the few countries that have large borate deposits and processing plants, conduct of a study of human exposure in this area is important.

The purpose of this study was to investigate of borates;

- Reproductive effects,
- Developmental effects,
- Effects on the sex ratio

on environmentally and occupationally exposed male workers' families in a cross-sectional design.

Material and Methods

This work was conducted in three regions where boron plant are present in Turkey. Region I

gelişimsel etkiler bakımından belirgin farklılık yoktur. Sonuç olarak 3 bölgedeki işçilerin maruz kaldığı bor düzeyinin re-
produktif özellikleri etkilemediği görülmüştür.

Anahtar Kelimeler: Bor, Fertilite, İşçiler

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was Bigadiç county of the province Balıkesir. Region II was Emet-Hisarçik county of the province Kütahya and Region III was Kirka county of the province Eskişehir. In Bigadiç, colemanite and ulexite (Ca borate and Na-Ca borate respectively), in Emet-Hisarçik colemanite, in Kirka tincal and borax pentahydrate are produced by Etibank company. The boron level in drinking water ranges from 1.7 to 9.4ppm for Region I, from 2.79 to 5.94 in Region II and from 0.36 to 0.62 in Region III according to some measurements of Etibank company in this region. In production departments, dust concentration varied from 1.11 to 2.96 mg/m³ in Region I, 0.69 to 9.25 mg/m³ in Region II and 0.39 to 9.47 mg/m³ in Region III. Our study population was married male workers from these three boron plants. Total number of workers from three plants was 1730 and we selected 850 workers by random sampling methods. The number of workers that have been contacted was 799. 642 of them were production workers and others (157) were office workers. Data was collected by personal interviews of workers at their work place in 1998. SPSS for Windows software package and Chi-square and Student's t test are used for data analysis and statistics.

Definition of primary infertility was: "No visual evidence of a conceptus in a non-parous, monogamous, pre- menopausal person who maintained conjugal relationship for at least 9 months prior and after neither partner used any type of birth control method for the preceding 12 months."

Definition of secondary infertility was: " No visual evidence of a conceptus in a parous, monogamous, pre- menopausal person who maintained

Table 1. The social and demographic characteristics and the work assignment in company for the workers from three regions

Socio-demographic characteristics and work status	Region I (Bigadiç) n=328	Region II (Emet-Hisarcik) n=298	Region III (Kırka) n=173	Total n=799
Average Age (±SD)	39.44 ± 4.29	36.64 ± 7.35	36.35 ± 6.70	37.73±6.27
Place of birth n (%)				
Boron place	126(38.4)	150(50.3)	76(43.9)	352(44.1)
Boron free place	202(61.6)	148(40.7)	97(56.1)	447(55.9)
Average duration in boron places (±SD) (year)	21.39 ± 14.99	29.37 ± 13.14	19.85 ± 16.30	23.56±15.25
Level of education n (%)				
Primary school	230(70.1)	130(43.6)	69(39.9)	429(53.8)
Secondary school	29(8.8)	54(18.1)	20(11.6)	103(12.9)
High school	63(19.2)	94(31.5)	73(42.2)	230(28.8)
University	6(1.8)	20(6.7)	11(6.4)	37(4.6)
Income per worker per year (in million TL) (±SD)	368.34 ± 140.52	346.15 ± 153.09	366.07 ± 187.11	359.58±156.42
Work assignment (%)				
Production workers	295(89.1)	198(66.4)	149(86.1)	642(80.3)
Office workers	33(10.1)	100(33.6)	24(13.9)	157(19.7)
Average duration of production work (±SD) (year)	13.27 ± 7.25	10.34± 7.67	10.26 ± 7.10	11.72±7.48

conjugal relationship for at least 9 months prior and after neither partner used any type of birth control method for the preceding 12 months."

Results

A total number 799 married male workers from three boron plants, 378 from Region I (Bigadiç), 298 from Region II (Emet-Hisarcik) and 173 from Region III (Kırka), that are exposed to boron with occupational reasons as well as with environmental reasons due to the level of boron in water in these regions are included in the study.

The age, the place of birth, the duration of residence in the regions where boron is present, the level of education, the level of income and work assignment in company are shown in Table 1.

Marital status for the workers is shown in Table 2.

Fertility:

The primary infertility rate is determined as 1.2% for Region I, 1% for Region II and 4.1% for Region III upon evaluation of the reproductive

characteristics for the workers included in the study (Table 3).

The mean number of children for the workers already with children is 2.48 ± 0.91 for Region I (n = 316), 2.27 ± 1.04 for Region II (n = 269) and 2.40 ± 0.91 for Region III (n = 151). The mean duration from the birth of the last child is 10.46 ± 4.93 for Region 1, 9.11 ± 5.84 for Region II and 8.07 ± 5.24 for Region III.

The reproductive characteristics of workers after the birth of the last child is shown in Table 4. The ratio of workers not using birth control methods since the birth of the last child and yet unable to give birth to a child more than one year, is 4.1 % for Region I, 3.7 % for Region II, none for Region III and 3.1% for total. These ratios can be assumed as possible secondary infertility rates. These couples can be evaluate later.

Sex Ratio:

Furthermore, male to female ratio at birth has been evaluated for the worker couples (Table 5). It was 1.2 for whole group.

Table 2. Marital characteristics for the workers

Some marital characteristics	Region I (Bigadic) n=328	Region II (Emet-Hisarcik) n=298	Region III (Kirka) n=173	Total n=799
Average age at marriage (±SD) (year)	22.14 ±3.40	21.66 ±2.91	22.84 ± 3.26	22.12±3.23
Average duration of marriage(±SD)(year)	17.12 ±5.65	14.81 ±8.43	13.46 ±7.63	15.46±7.36
Consanguinity status with partner n (%)				
Distant	27(8.2)	41(13.8)	10(5.8)	78(9.8)
Close	36(11.0)	48(16.1)	15(8.7)	99(12.4)
Not present	265(80.8)	209(70.1)	148(85.5)	622(77.8)

Table 3. Reproductive characteristics for the workers

Reproductive characteristics	Region I (Bigadic) n=328(%)	Region II (Emet-Hisarcik) n=298 (%)	Region III (Kirka) n=173(%)	Total n=799(%)
With children	316(96.3)	269(90.3)	152(87.9)	737(92.2)
Pregnant	3(0.9)	9(3.0)	6(3.5)	18(2.2)
Recently married	1(0.3)	12(4.0)	7(4.0)	20(2.5)
Users the birth control methods	3(0.9)	4(1.3)		7(0.9)
Habitual abortion	1(0.3)	1(0.3)	1(0.6)	3(0.4)
Infertility characteristics				
Infertile female	1(0.3)	3(1.0)	2(1.2)	6(0.8)
Infertile male	2(0.6)		4(2.3)	6(0.8)
Infertile female and infertile male			1(0.6)	1(0.1)
Cause for infertility undetermined	1(0.3)			1(0.1)
Infertility Rates: <i>(Inf. female+Inj. male+ Both inf.+ cause undetermined)</i>	1.2%	1%	4.1%	1.8%

Table 4. The reproductive characteristics of workers after last child for the workers already with children

Reproductive characteristics after the last child	Region I (Bigadic) n=316(%)	Region II (Emet-Hisarcik) n=269(%)	Region III (Kirka) n=151(%)	Total n=736
Users the birth control methods	291(92.1)	235(87.4)	140(92.7)	666(90.5)
Pregnancy	7(2.2)	16(5.9)	7(4.6)	30(4.1)
Partner in menopause	5(1.6)	7(2.6)	4(2.7)	16(2.2)
Absence of birth control method (<1 year)		1(0.4)		1(0.1)
Absence of birth control method (1 year)	13(4.1)	10(3.7)		23(3.1)

Developmental Effects:

In attempt to determine the possible developmental effects of exposure to boron, live births as well as stillbirths, spontaneous abortions and premature births with low birth weight have been

evaluated (Table 6).

Neonatal mortality proportion, postneonatal mortality proportion and infant mortality proportion for worker couples are shown in Table 7 These proportions reflect high rates of past years

Table 5. The number of all male children and all female children at birth for the worker couples.

Sex (Live Birth)	Region I (Bigadiç) n(%)	Region II (Emet-Hisarçık) n (%)	Region III (Kırka) n(%)	Total n(%)
Male	443(51.75)	369(53.79)	211(53.83)	1023(52.9)
Female	413(48.25)	317(46.21)	181(46.17)	911(47.1)
Total	856(100.0)	686(100.0)	392(100.0)	1934(100.0)
Male/Female Ratio:	1.07	1.16	1.17	1.12

Table 6. Findings possible associated developmental effects

Outcomes of pregnancies	Region I (Bigadiç)		Region II (Emet-Hisarçık)		Region III (Kırka)		Total	
	Number of couples n=328 Per Couple pregn.	Number of pregnancies n=1096 Per 100	Number of couples n=298 Per Couple pregn.	Number of pregnancies n=875 Per 100	Number of couples n=173 Per Couple pregn.	Number of pregnancies n=535 Per 100	Number of couples n=799 Per Couple pregn.	Number of pregnancies n=2506 Per 100
Live births	2.61	78.10	2.30	78.40	2.27	73.27	2.42	77.17
Stillbirths	0.05	1.64	0.09	3.09	0.05	1.68	0.07	2.15
Premature births or low birth weights	0.14	5.25*	0.12	5.24*	0.13	5.60*	0.13	5.33*
Spontaneous abortions	0.23	6.75	0.21	7.31	0.28	8.97	0.23	7.42

* .Per 100 live births

X

Table 7. Neonatal mortality proportion, postneonatal mortality proportion and infant mortality proportion per 1000 live births

Mortality	Region I (Bigadiç) Number of live births n=856 Per 10 ³	Region II (Emet-Hisarçık) Number of live births n=686 Per 10 ³	Region III (Kırka) Number of live births n=392 Per 10 ³	Total n=1934 Per 10 ³
Neonatal mortality	29.21	34.99	30.61	31.54
Postneonatal mortality	38.55	56.85	35.71	44.47
Infant mortality	67.76	91.84	66.32	76.01

Work Assignment and Reproductive Characteristics:

After the whole workers are grouped according to work assignment, they are compared for reproductive characteristics (Table 8). Average pregnancy and average live-birth were significantly higher in the production workers than the officers. Other characteristics didn't show any relation with work assignment.

Discussion

The workers in three boron plants in which this study has been conducted are residents of the same regions. The level of boron in water has been found to be higher for Region I and Region II and lower for Region III. The workers have been living for 19 to 29 years in the region where boron is present and have similar social and demographic characteristics. Social and demographic characteristics of the workers didn't differ radically from any other pop-

Table 8. Comparison of reproductive characteristics and work assignment

Some reproductive characteristics	Work Assignment		p
	Production workers n=642	Office workers n=157	
Primary infertile n(%)	10(1.6)	4(2.5)	0.397
Others	632(98.4)	153(97.5)	
Secondary infertile n(%)	20(3.3)	3(2.2)	0.784 »
Others	580(96.7)	133(97.3)	
Male	846(53.11)	177(51.91)	0.687
Female	747(46.89)	164(48.09)	
Average pregnancy	3.2	2.8	0.034*
Average live birth	2.4	2.1	0.008**
Average stillbirth	0.07	0.04	0.345
Average sp. abortions	0.24	0.18	0.220
Average prem./Low Birth W.	0.12	0.14	0.545
Average neonatal mortality	0.07	0.08	0.562
Average postneonatal mortality	0.11	0.11	0.980

* $p < 0.05$ ** $p < 0.01$

ulation in Turkey (12). Production workers have worked for average 10 years or more in the production part of boron plant. They are more directly exposed to boron than the office workers because of boron dust in their departments. The average age at marriage for the workers range from 21 to 22 years and it was similar with marriage age of men in Turkey which is 22 years old and the workers have been married for 13 to 17 years. Ratio of consanguinity status with partner was similar to general status of Turkish population (13).

The infertility rate has been determined as 1.2% for Region I, 1.0% for Region II and 4.1% for Region III. These rates seem to be not related with the levels of boron in water in the corresponding regions. Even though infertility rate was highest in Region III which has the lowest boron level in water. When the workers are evaluated as the whole group, the infertility rate is determined as 1.8%. These results are consistent with the results of previous studies conducted in the same regions (9). The infertility rate has been determined as 2% in a study conducted on the population living in the same regions in the absence of exposure to boron with occupational reasons (14).

The infertility rates that have been determined in this study do not differ upon comparison either from the infertility rate for Turkey in general or from the infertility rates for those regions where boron is present. The infertility rate for Turkey in

general for women between 45 to 49 years of age is 2.2% (15). Infertility rates for regions where boron is not present, as obtained from localized studies, range from 1.49 to 3.8% (16,17). The ratio of secondary infertile worker couples is 4.1% for Region I, 3.7% for Region II and none for Region III. This ratio is 3.1% for total and these couples will later be evaluated.

Upon evaluation of the male to female ratio at birth for the worker couples, no increase in the number of female children at birth has been observed as reported in the literature (8). These male to female ratios are similar to those reported from around the world and those reported from Turkey concerning an unaffected population. Male/female ratio is 1.05-1.08 in Turkey (15). In this study we found that ratio as 1.12 so we didn't observe any increase in female children. Average livebirths for 15-49 years old women is 2.01 in Turkey. In our study livebirths of workers (2.42) were not lower.

In a similar study conducted in Ankara on a population in the absence of exposure to boron (18), the number of stillbirths Per couple has been determined as 0.05, this was equal to the number of stillbirths Per worker couple for Region I and III. It was 0.09 in Region II. Stillbirths were 1.5 Per 100 pregnancies in Turkish demographic and health survey (115). We found that stillbirths Per 100 pregnancies, 1.64 for Region I, 1.68 for Region III, but 3.09 for Region II. The number of premature

births or low birth weight per couple in the above mentioned study in Ankara (18) has been determined as 0.26 higher than 0.14, 0.12 and 0.11 for Region I, Region II and Region III, respectively. So we can say that there is no increase of premature births or low birth weights for these regions. Spontaneous abortion is 8.7 Per 100 pregnancies for Turkey in General (15). It is very similar ratios with 6.75, 7.31 and 8.97 for three regions.

The infant mortality rate has been determined as 63 per 1000 live births in Ankara, similar to the infant mortality rate for Region I(67.7) and Region II(66.3) but not to Region III(91.8). Region II has the highest mortality rate but doesn't have highest exposure to boron, because of the moderate boron level in water. Also in Region II production workers are not more than other regions. So we can think that there are some other reasons for this differences. The differences between the regions are the reflections of the social and cultural structure. According to our observations people in Region II have lower social and cultural level than Region I and III. But the difference between three regions were not statistically significant. Although the infant mortality rate for Turkey has fallen down to 43 per 1000 live births (15), the infant mortality rate that have been cited in the study belong to an older generation, therefore, are not current rates and it reflects the high rates of past years.

In conclusion, exposure to boron can be stated not to adversely influence the infertility ratio, the male to female ratio at birth, the number of stillbirths, the number of spontaneous abortions, the number of premature births with low birth weight and the infant mortality rate for the workers from three boron plants.

Primary infertility, secondary infertility, sex ratio, stillbirth, prematurity/low birth weight, spontaneous abortions and infant mortality didn't show any relation with work assignment. Moreover average pregnancy and average live birth was significantly higher in the production workers than the officers. But production workers were older and had longer period after marriage. This difference may be based on this situation. So we can say that boron exposure didn't effect production workers for reproductive characteristics in negative direction.

REFERENCES

1. Linder RE, Strader LF, and Rehnberg GL. Effect of acute exposure to boric acid on the male reproductive system of the rat. *J Toxicol Environ Health* 1990; 31; 133-46.
2. Weir RJ and Fisher RS. Toxicologic studies on borax and boric acid. *Toxicol Appl Pharmacol* 1972; 23;351-64.
3. Lee IP, Sherins RJ, and Dixon RL. Evidence for induction of germinal aplasia in male rats by environmental exposure to boron. *Toxicol Appl Pharmacol* 1978; 45;577-90.
4. Fail PA, George WD, Seely JC, Grizzle TB, and Heindel JJ. Reproductive toxicity of boric acid in Swiss (CD-1) mice: assessment using the continuous breeding protocol. *Fundam Appl Toxicol* 1991; 17;225-39.
5. Ku WW, Chapin RE, Wine RN, and Gladen BC. Testicular toxicity of boric acid (BA); Relationship of dose to lesion development and recovery in the F344 rat. *Reprod Toxicol* 1993; 7;305-19.
6. Tarasenko N Yu, Kasparov AA, and Strongina OM. Effect of boric acid on the generative function in males. *Gigiena Truda i Professionalnye Zabolevaniya* 1972; 11; 13-6.
7. Krasowski GN, Varshavskaya SP, and Borisov AI. Toxic and gonadotropic effects of cadmium and boron relative to standards for these substances in drinking water. *Environ Health Perspect* 1976; 13:69-75.
8. Whorton MD, Haas JL, Trent L, Wong O. Reproductive effects of sodium borates on male employees: birth rate assessment. *Occup Environ Med* 1994; 51;761-7.
9. Şayli BS, Tüccar E, Elhan AH. An assessment of fertility in boron-exposed Turkish subpopulations. *Reproductive Toxicology* 1998; 12(3);297-304.
10. Heindel JJ, Price CJ, Field EA, Marr MC, Myers CB, Morissey RE and Schwetz BA. Developmental toxicity of boric acid in mice and rats. *Fundam Appl Toxicol* 1992; 18;266-77.
11. Price CJ, Marr MC, and Myers CB. Determination of the NOAEL for developmental toxicity in Sprague-Dawley rats exposed to boric acid in feed on gestational days 0 to 20, and evaluation of postnatal recovery through postnatal day 21. Report 65C-5657-200. Research Triangle Park NC, USA 1994.
12. State Institute of Statistics Prime Ministry Republic of Turkey - Statistical Year-Book (1998).
13. Health Ministry - Hacettepe University Institute of Population Studies, Turkish demographic and health survey 1993.
14. Çöl M, Gene Y, Erçevik E. Assessment of fertility in boron exposed Turkish subpopulations Medical Network J Clin Science Doctor (In press).
15. Health Ministry - Hacettepe University Institute of Population Studies, Turkish demographic and health survey 1998.
16. Çetinkaya F, Aykut M, Ozturk Y 15-49 age group married officers and labor women's knowledge attitude and behaviors about family planning. IV. National Public Health Congress, Abstract book, pp: 106-9 Turkey 1994.
17. Çivi S, Yayci M. Infertility prevalences and causes. IV. National Public Health Congress, Abstract book, Turkey 1994; 53-6.
18. Çöl M, Çalışkan D, Akdur R. Fertility characteristics and use of contraceptives in Park Health Centre Region. *Turkish Republic Health Ministry, Health Journal* 1996; 67(1-2):50-62.