Supplemental Tables

The association between urinary concentrations of phosphorous-containing flame retardant metabolites and semen parameters among men from a fertility clinic

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Supplemental Table 1. Crude bivariate associations with PFR and semen parameters among (n=220) men

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Metabolite | | | | | | | | | | | |
|  | BDCIPP | | | | DPHP | | | ip-PPP | | | tb-DPHP | | |
| Semen parameters | r | 25th, 75th % | | p-Value | r | 25th, 75th % | p-Value | r | 25th, 75th % | p-Value | r | 25th, 75th % | P-Value |
| Total sperm count | 0.06 |  | 0.36 | | 0.08 |  | 0.34 | 0.07 |  | 0.37 | 0.08 |  | 0.67 |
| Concentration (mil/mL) | 0.10 |  | 0.14 | | 0.06 |  | 0.36 | 0.07 |  | 0.83 | 0.11 |  | 0.56 |
| Motility (P+NP) (%) | **0.16** |  | 0.02 | | 0.08 |  | 0.23 | 0.04 |  | 0.61 | 0.11 |  | 0.55 |
| Progressive motility | **0.15** |  | 0.04 | | 0.04 |  | 0.61 | 0.06 |  | 0.46 | 0.13 |  | 0.51 |
| Morphology (%norm) | 0.09 |  | 0.21 | | -0.02 |  | 0.82 | 0.05 |  | 0.55 | 0.29 |  | 0.12 |
| Sample volume (mL) | -0.05 |  | 0.45 | | -0.05 |  | 0.43 | 0.004 |  | 0.96 | 0.14 |  | 0.45 |
|  |  |  |  | |  |  |  |  |  |  |  |  |  |
| Total sperm count   <39 mill a Yes  No | 0.50 0.62 | 0.35, 0.76  0.35, 1.46 | 0.13 | | 0.72 0.76 | 0.34, 1.86 0.41, 1.47 | 0.81 | 0.35 0.36 | 0.12, 0.83 0.21, 0.62 | 0.55 | 0.13 0.12 | 0.13, 0.13 0.12, 0.22 | 0.51 |
| Sperm concentration  <15 mil/mL a Yes  No | 0.46 0.62 | 0.35, 0.79 0.35, 1.16 | 0.21 | | 0.67 0.77 | 0.29, 0.93 0.42, 1.48 | 0.21 | 0.30 0.37 | 0.13, 0.64 0.21, 0.64 | 0.26 | 0.38 0.16 | 0.38, 0.38 0.12, 0.20 | 0.22 |
| Percent motile sperm  (P+NP) <40 a  Yes  No | 0.55 0.72 | 1.11 1.67 | 0.08 | | 0.73 0.74 | 0.37, 1.37 0.42, 1.47 | 0.68 | 0.36 0.39 | 0.21, 0.59 0.19, 0.64 | 0.69 | 0.16 0.16 | 0.12, 0.20 0.12, 0.25 | 0.80 |
| Percent morph.  Sperm <4 a Yes  No | 0.62 0.61 | 0.36, 1.26 0.34, 1.45 | 0.92 | | 0.77 0.74 | 0.44, 1.32 0.41, 1.47 | 0.82 | 0.36 0.40 | 0.20, 0.79 0.21, 0.64 | 0.95 | 0.15 0.18 | 0.13, 0.16 0.13, 0.24 | 0.21 |

r= spearman coefficient; a r = median values, p-value for 2-tailed test

Supplemental Table 2. Bivariate associations of PFR metabolite (uncorrected) and demographic characteristics (n=220 men)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Metabolite | | | | | | | | | | | | |
|  | BDCIPP | | | DPHP | | | | ip-PPP | | | tb-DPHP | | |
| Demographic characteristic | r | 25th, 75th % | P-value | r | 25th, 75th % | P-value | r | | 25th, 75th % | P-value | r | 25th, 75th % | P-value |
| Age | -0.04 |  | 0.54 | -0.01 |  | 0.81 | 0.03 | |  | 0.69 | -0.15 |  | 0.38 |
| BMI | 0.21 |  | **0.0005** | 0.08 |  | 0.15 | 0.04 | |  | 0.49 | -0.09 |  | 0.59 |
| Abstinence period | 0.07 |  | 0.27 | 0.01 |  | 0.89 | 0.08 | |  | 0.26 | 0.14 |  | 0.45 |
|  |  |  |  |  |  |  |  | |  |  |  |  |  |
| Race a  White  Black  Asian  Other | 0.60 0.99 0.52 1.65 | 0.30, 1.29 0.76, 1.06 0.38, 2.50 0.81, 2.34 | 0.08 | 0.74 0.53 1.23 1.02 | 0.41, 1.28 0.25, 0.65 0.55, 1.69 0.73, 1.48 | 0.20 | 0.35  0.97 0.24 0.30 | | 0.20, 0.61 0.08, 1.51 0.13, 0.40 0.15, 0.62 | 0.38 | 0.16 0.23 0.16 0.18 | 0.09, 0.20 0.23, 0.23 0.09, 0.26 0.18, 0.18 | 0.71 |
| Smoking Status a  Never smoke  Past smoker  Current smoker | 0.62 0.55 0.58 | 0.30, 1.46 0.37, 1.41 0.30, 0.83 | 0.71 | 0.74 0.76 0.79 | 0.39, 1.28 0.53, 1.50 0.46, 1.26 | 0.67 | 0.34 0.36 0.35 | | 0.19, 0.62 0.20, 0.64 0.23, 0.52 | 0.91 | 0.16 0.18 - | 0.10, 0.20 0.07, 0.23 | 0.75 |
| Education a  <High school  HS grad  1 or 2 yr. college  3 or 4 yr. college  College grad  Graduate degree | 2.66 0.93 0.48 0.74 0.60  0.48 | 0.56, 3.30 0.22, 1.52 0.26, 0.81 0.43, 1.45 0.38, 1.15 0.27, 0.13 | 0.15 | 0.58 1.50  1.30 0.68 0.74  0.73 | 0.58, 1.02 0.48, 4.32 0.54, 2.19 0.47, 1.08 0.41, 1.24 0.34, 1.22 | 0.51 | 0.36 0.45 0.38 0.47 0.30  0.33 | | 0.24, 0.48 0.35, 0.62 0.31, 0.47 0.19, 0.63 0.16, 0.52 0.18, 0.54 | 0.61 | -  -  0.16 - 0.16 0.19 | - - 0.16, 0.16 - 0.13, 0.17 0.07, 0.26 | 1.00 |
| Season a  Winter  Spring  Summer  Fall | 0.54 0.44 1.04 0.60 | 0.22, 0.98 0.29, 0.75  0.52, 1.81  0.28, 1.12 | **<0.0001** | 0.89 0.71 0.75 0.72 | 0.54, 1.94 0.34, 1.26 0.45, 1.54 0.37, 1.03 | 0.05 | 0.38 0.34 0.34  0.35 | | 0.17, 0.54 0.19, 0.63 0.21, 0.77 0.20, 0.54 | 0.80 | 0.15 0.17 0.16 0.17 | 0.10, 0.23 0.10, 0.23 0.09, 0.20 0.12, 0.22 | 0.96 |

r= Spearman coefficient; a r = median values; Winter: December-February, Spring: March-May; Summer: June-August; Fall: September-November

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Metabolite a | | | | | | | | | | | |
|  | BDCIPP | | | DPHP | | | ip-PPP | | | ∑ PFR | | |
| Sperm Parameter | β | 95%CI | p-Value | β | 95%CI | p-Value | β | 95%CI | p-Value | β | 95%CI | p-Value |
| Total sperm count a, b | -0.04 | (-0.14, 0.07) | 0.49 | 0.05 | (-0.07, 0.17) | 0.42 | -0.0001 | (-0.11, 0.00) | 1.00 | 0.07 | (-0.07, 0.21) | 0.33 |
| Concentration (mil/mL) a, c | -0.001 | (-0.11, 0.10) | 0.91 | 0.06 | (-0.05, 0.17) | 0.28 | 0.04 | (-0.07, 0.14) | 0.49 | 0.09 | (-0.04, 0.23) | 0.17 |
| Motility (P+NP) (%) a, c | 0.07 | (-0.02, 0.17) | 0.11 | 0.07 | (-0.04, 0.16) | 0.22 | 0.04 | (-0.06, 0.14) | 0.40 | 0.14 | (-0.02, 0.29) | 0.08 |
| Progressive motility a, d | 0.07 | (-0.04, 0.17) | 0.21 | 0.06 | (-0.06, 0.17) | 0.32 | 0.06 | (-0.05, 0.17) | 0.29 | 0.11 | (-0.03, 0.25) | 0.12 |
| Morphology (%norm) e | 0.32 | (-0.07, 0.72) | 0.11 | 0.22 | (-0.26, 0.70) | 0.36 | 0.26 | (-0.19, 0.711) | 0.25 | 0.41 | (-0.17, 0.99) | 0.16 |
| Sample volume (mL) f | -0.10 | (-0.26, 0.06) | 0.20 | -0.08 | (-0.26, 0.11) | 0.42 | -0.06 | (-0.24, 0.11) | 0.47 | -0.16 | (-0.39, 0.06) | 0.16 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Odds Ratio | OR |  |  | OR |  |  | OR |  |  | OR |  |  |
| Total sperm count <39 mill b | 0.85 | (0.63, 0.85) | 0.33 | 0.90 | (0.59, 1.39) | 0.65 | 1.01 | (0.55, 1.84) | 0.98 | 0.71 | (0.45, 1.12) | 0.39 |
| Sperm concentration <15 mil/mL c | 0.88 | (0.64, 1.22) | 0.44 | 0.91 | (0.57, 1.48) | 0.70 | 0.98 | (0.53, 1.79) | 0.94 | 0.74 | (0.41, 1.34) | 0.39 |
| Percent motile sperm (P+NP) <40 b | 0.94 | (0.72, 1.22) | 0.64 | 0.92 | (0.67, 1.27) | 0.62 | 0.92 | (0.66,1.28) | 0.64 | 0.76 | (0.52, 1.12) | 0.17 |
| Percent morph. Sperm <4 e | 0.89 | (0.65, 1.20) | 0.43 | 1.00 | (0.72, 1.39) | 0.99 | 0.92 | (0.65, 1.31) | 0.64 | 0.81 | (0.51, 1.27) | 0.34 |

Supplemental Table 3. Regression coefficients and odds ratios (95% CI) for semen parameters of men contributing (1-5) urine samples restricting 1.01 ≤ SG ≤ 1.03. Adjusted for specific gravity, age, BMI, smoking status & abstinence period

a natural log transformation; b n=168; c n=188; d n=185; e n=204; f n=214

Supplemental Table 4. Intraclass correlation coefficients (95% CI) for repeated semen parameters

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | Subjects | Observations | ICC | 95% CI |
| Total sperm count (mill) | 174 | 235 | 0.52 | (0.36, 0.67) |
| Concentration (mil/mL) | 176 | 237 | 0.58 | (0.41, 0.74) |
| Motility (P+NP) (%) | 176 | 237 | 0.79 | (0.69, 0.86) |
| Progressive motility | 173 | 234 | 0.71 | (0.58, 0.81) |
| Morphology (%norm) | 189 | 255 | 0.51 | (0.35, 0.66) |
| Sample volume (mL) | 195 | 267 | 0.58 | (0.43, 0.71) |

Supplemental Table 5. Odds ratios (95% CIs) by quartile of PFR metabolite for males contributing 1-5 samples. Adjusted for

specific gravity, age, BMI, smoking status & abstinence period

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Semen parameters | | | | | | | | | | |
| PFR a | (quartile range) | Total sperm count  (<39 x 106) | | Sperm Concentration  (<15 million/mL) | | | Sperm motility  (<40% motile sperm) | | | Morphology  (<4% normal) | | |
| BDCIPP |  |  | | | | | | | | | | |
| Q1 | (0.2-0.17) | - | | | - | | | - | | | - | |
| Q2 | (0.18-0.51) | 1.99 | (0.65 6.14) | | 1.04 | (0.38, 2.86) | | 0.69 | (0.34, 1.36) | | 1.74 | (0.79, 3.82) |
| Q3 | (0.52-1.11) | 1.24 | (0.03, 59.36) | | 2.79 | (0.05, 144.68) | | 0.21 | (0.02, 2.96) | | 1.38 | (0.08, 23.06) |
| Q4 | (1.12-10.30) | 0.16 | (0.02, 1.42) | | 0.35 | (0.05, 2.58) | | 0.99 | (0.27, 3.58) | | 0.41 | (0.08, 2.03) |
| p-trend |  | 0.14 | | | 0.25 | | | 0.91 | | | 0.38 | |
| DPHP |  |  | | | | | | | | | | |
| Q1 | (0.07-0.27) | - | | | - | | | - | | | - | |
| Q2 | (0.28-0.65) | 1.50 | (0.32, 1.07) | | 1.15 | (0.30, 4.42) | | 1.48 | (0.57, 3.87) | | 0.63 | (0.20, 1.97) |
| Q3 | (0.66-1.21) | 0.55 | (7.90x10-5, 3847.58) | | 0.27 | (1.03, 700.36) | | 0.13 | (9.42x10-4, 18.52) | | 6.79x10-4 | (1.72x10-6, 0.27) |
| Q4 | (1.22-10.57) | 1.04 | (0.20, 5.31) | | 0.71 | (0.07, 6.97) | | 0.76 | (0.20, 2.95) | | 2.33 | (0.40, 13.73) |
| p-trend |  | 0.83 | | | 0.91 | | | 0.96 | | | 0.24 | |
| ip-PPP |  |  | | | | | | | | | | |
| Q1 | (0.04-0.08) | - | | | - | | | - | | | - | |
| Q2 | (0.09-0.18) | 0.78 | (0.43, 1.40) | | 1.02 | (0.64, 1.62) | | 1.07 | (0.76, 1.49) | | 0.89 | (0.60, 1.34) |
| Q3 | (0.19-0.45) | 3.19 | (0.71, 14.36) | | 2.70 | (0.76, 9.53) | | 0.93 | (0.48, 1.81) | | 1.07 | (0.49, 2.36) |
| Q4 | (0.46-4.56) | 0.15 | (8.92x104, 26.62) | | 1.33 | (0.01, 150.55) | | 1.53 | (0.08, 31.26) | | 2.02 | (0.08, 52.44) |
| p-trend |  | 0.97 | | | 0.60 | | | 0.93 | | | 0.50 | |
| ∑PFR |  |  | | | | | | | | | | |
| Q1 | (0.17-0.79) | - | | | - | | | - | | | - | |
| Q2 | (0.80-1.86) | 1.60 | (0.01, 502.90) | | 1.87 | (0.01, 298.90) | | 1.02 | (0.04, 29.15) | | 2.06 | (0.04, 104.27) |
| Q3 | (1.87-3.21) | 1.57 | (0.32, 7.71) | | 1.74 | (0.42, 7.26) | | 0.71 | (0.27, 1.85) | | 1.48 | (0.45, 4.83) |
| Q4 | (3.22-15.56) | 0.79 | (0.33, 1.86) | | 0.54 | (0.20, 1.50) | | 0.76 | (0.45, 1.29) | | 0.79 | (0.37, 1.71) |
| p-trend |  | 0.70 | | | 0.32 | | | 0.24 | | | 0.50 | |

a natural log transformation; Quartile 1=reference