Changes in the semen quality among 5739 men seeking infertility treatment in Northern Norway over past 20 years (1993–2012)

Purusotam Basnet¹,², Sissel A Hansen¹, Inger K Olaussen¹, Martha A Hentemann¹,² and Ganesh Acharya¹,²

Abstract
Semen quality plays a pivotal role in sustaining the fertility rate and healthy population growth. Therefore, assessment of temporal trends in the semen quality provides valuable public health information. We analyzed the semen quality parameters of 5739 North Norwegian men among consecutive couples attending the fertility clinic of University Hospital of North Norway for investigation and/or treatment from 1993 to 2012. The seminal fluid volume, sperm concentration, and total sperm count were found to have gradually decreased during the past 20 years. The proportion of hypospermic, azoospermic, and oligozoospermic men had increased by 24.6% (p < 0.001), 109.5% (p < 0.001), and 9.5% (p = 0.05), respectively, in the last decade (2003–2012) compared to the first decade (1993–2002). The parameters of semen quality are rapidly deteriorating in North Norwegian men seeking fertility treatment.

Keywords
Semen quality, hypospermia, oligozoospermia, azoospermia, North Norway

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Introduction
The semen quality is one of the fundamental determinants of reproductive success and well-being of future generation. Reports on the semen quality have been frequently published over the past several decades from different countries. A meta-analysis by Carlsen et al. (1992), which included 61 studies from all six continents during 50 years (1940–1990), initiated a debate among scientists and drew attention of the general population and politicians (Bromwich et al., 1994; Farrow, 1994). Reports on temporal trends in semen quality based on semen volume, sperm concentration, motility, and morphology have remained controversial since partly opposite conclusions were drawn using same data but alternative models for statistical analysis (Becker and Berhane, 1997; Olsen et al., 1995). Some studies have shown a decline in the semen volume and/or sperm cell concentration, motility, and morphology (Adampoulos et al., 1996; Auger et al., 1995; Geoffroy-Siraudin et al., 2012; Irvine et al., 1996; Van Waeleghem et al., 1996; Younglai et al., 1998), while other similar studies have provided the opposite conclusion (Bujan et al., 1996; Fisch et al., 1996; Itoh et al., 2001; Paulsen et al., 1996; Rasmussen et al., 1997; Vierula et al., 1996). Several factors such as the genetic factors, environmental exposure, changes in lifestyle and food habit, oxidative stress, geographical distribution, and so on have been

¹ IVF Unit, Department of Obstetrics and Gynecology, University Hospital of North Norway, Tromsø, Norway
² Women’s Health and Perinatology Research Group, Department of Clinical Medicine, Faculty of Health Sciences, UiT-The Arctic University of Norway, Tromsø, Norway

Corresponding author:
Purusotam Basnet, IVF Unit, Department of Obstetrics and Gynecology, University Hospital of North Norway, 9038 Tromsø, Norway.
Email: purusotam.basnet@uit.no
suggested to be associated with the changes in semen profile, however, no conclusive evidence has been found. Decline in semen quality may lead to a parallel increase in male infertility and subsequently demographic changes. Therefore, it is important to assess trends in semen quality. The objective of this study was to evaluate the temporal trends in semen quality using routinely collected clinical laboratory data of 5739 men who attended the fertility clinic of the University Hospital of North Norway over the past 20 years.

Materials and methods

Study population

The laboratory records and reports on semen analysis of all men who attended the fertility clinic of the University Hospital of North Norway from 1993 to 2012 were studied. The fertility clinic (IVF Unit) was established within the Department of Obstetrics and Gynecology in 1984. Semen analysis was performed as a routine procedure during the clinical investigation of subfertile/infertile couples. Complete records were available from 1993 onward. All subjects included in the study resided in the Northern region of Norway during the time of semen analysis. The study was considered as a quality assurance project not requiring Ethics Committee approval. The analysis of routinely collected clinical and laboratory data was approved by the data protection authority of the hospital (ref. 2015/2856).

Method of semen analysis

Men received both oral and written instructions and were requested to produce and submit a fresh semen sample after 3–5 days of sexual abstinence. Semen was analyzed using the conventional techniques adapted from the methods described in the third, fourth, and fifth editions of the World Health Organization (WHO) laboratory manuals (WHO, 1987, 1992, 2010) and the data were recorded according to hospital protocol. The protocol for measuring the volume, concentration, motility, and morphology of semen/sperm cells has not been changed significantly during the past 20 years. Semen volume was measured with a 5 mL plastic pipette, but in some cases, micropipette or 10 mL plastic pipette was also used. Sperm concentration and motility were assessed by direct observation of semen under a microscope after appropriate dilution (WHO, 1987, 1992, 2010). Morphology was assessed after Papanicolaou staining and the aggregation was confirmed by mixed antibody reaction test for sperm cell antibodies.

Data analysis and statistics

The present study includes the results of all semen analyses performed at our laboratory over a period of 20 years. In some of the subjects, the semen analyses were carried out two or more times in the same year, and in such cases, the mean value per person was used for the purpose of statistical analysis. All analyses were performed by eight laboratory technicians using the same protocol. The percentage of motility was graded on a scale of 0–4; 3–4 for the spermatozoa that presented rapid progression along a linear track, 2 for slowly progressive or nonlinear, 1 for motile on the spot, and 0 for immotile. Morphology assessment was based on the criteria described in the WHO laboratory manuals (WHO, 1987, 1992, 2010). The measured seminal fluid volume of less than 1.5 mL was considered as hypospermia, the absence of spermatozoa observed in whole ejaculate as azoospermia, and the sperm cell concentration and total sperm cell count per ejaculate less than the reference values (15 × 10⁶ sperm cells/mL and 39 × 10⁶ sperm cells/ejaculate) as oligozoospermia. In addition to a yearly mean value of the seminal fluid volume, sperm cell concentration, and total sperm cell count per ejaculate, the mean values were also compared between the first decade (1993–2002) and the last decade (2003–2012). The proportion of hypospermia, azoospermia, and oligozoospermia were also compared between first and last decades. Data were analyzed using the SPSS 19.0 software (SPSS Inc. Chicago, Illinois, USA). Continuous variables are expressed as mean ± SD and categorical variables are reported as percentage. Temporal trends in semen characteristics were examined using a linear regression. The effect of men’s age and calendar year on semen characteristics was assessed using multiple regression models. Multiple coefficient of determination (R²) is presented along with p value. Independent sample t test was used to assess differences between groups. A two tailed p value of <0.05 was considered significant.

Results

The numbers of subjects varied each year from a minimum of 180 to a maximum of 389 with a total of 5739 in 20 years. The youngest person was 20 years old and the oldest was 63 years. The mean age of the men seeking fertility treatment during the study period increased gradually from 32.0 ± 5.1 years in 1993 to 35.0 ± 7.9 years in 2012 (R² = 0.755, p < 0.001), respectively (Table 1). The recorded minimum seminal fluid volume was 0.1 mL and the maximum was 13.0 mL. The maximum mean seminal fluid volume was 4.0 ± 1.9 mL (n = 281) in 1993 and the minimum mean seminal fluid volume was 2.7 ± 1.4 mL (n = 303) in 2011 (R² = 0.707, p = 0.002). A gradually decreasing trend of mean seminal fluid volume was observed during the study period (Table 1). The highest sperm count was 670.0 × 10⁶ sperm/mL. The maximum mean sperm cell count was 56.2 × 10⁶ sperm/mL (n = 360) in 1997 and a gradually decreasing trend was observed with the minimum mean sperm cell count of 35.9 × 10⁶ sperm/mL (n = 323) in 2009. A gradually decreasing trend of total sperm count per ejaculate was observed during the study period (R² = 0.660, p < 0.001). The mean total sperm cell count per ejaculate decreased from 189.9 × 10⁶ in 1993 (the highest) to 98.6 × 10⁶ (the lowest) in 2009 (R² = 0.892, p < 0.001; Table 1).

The mean seminal fluid volumes in the first decade (1993–2002) and the last decade (2003–2012) were 3.5 ± 1.7 (n = 2749) and 3.1 ± 1.5 mL (n = 2990), that is, a 11.4% decrease (p = 0.014). The mean sperm cell concentrations in the first decade (1993–2002) and the last decade (2003–2012) were 52.0 × 10⁶ and 40 × 10⁶ sperm/mL, respectively, that is, a 23.1% decrease (p < 0.001). The total sperm count in the first
decade was $166.0 \times 10^6$ sperms per ejaculate, which decreased by 28.9% ($p < 0.001$) in the last decade (Figure 1).

The distribution pattern of hypospermic, azoospermic, and oligozoospermic population from 1993 to 2012 is shown in Table 2. The proportion of hypospermic, azoospermic, and oligozoospermic population has been found to be in gradually increasing order from 1993 to 2012 among the north Norwegian men who approached the University hospital for the infertility treatment. The percentage of hypospermic and azoospermic population was found to be sharply increased than oligozoospermic men. The proportion of azoospermic men increased from 6.3% in the first decade to 13.2% in the last decade ($p < 0.001$). Similarly, the proportion of oligozoospermic men was 26.4% in the first decade, which increased by 9.5% ($p = 0.05$) to 28.9% in the last decade (Figure 3).

**Discussion**

Infertility pertains approximately 15% of sexually active couples and the quality of semen/sperms contributes significantly to the fertility potential. The total number of spermatozoa per ejaculate and the sperm cell concentration are related to time required to achieve pregnancy (Slama et al., 2002) as well as pregnancy rates (Zinaman et al., 2000) and are predictors of conception (Bonde et al., 1998; Larsen et al., 2000). Several factors such as man’s age, health status,
duration of his sexual abstinence before the collection of semen, and so on, can influence the characteristics of the semen (Jouannet et al., 1981; Schwartz et al., 1983). A wide variation in semen profile, expressed as the total number of spermatozoa and sperm cell concentration, was observed in a longitudinal study of five individuals who had semen analysis twice a month for one-and-a-half-year period (WHO, 2010).

In spite of individual variations, the present study clearly shows a gradual change of semen profile in our study population over two decades.

The mean seminal fluid volume (2.9 ± 0.1 mL) in the periods of last 4 years (2009–2012) was 26.0% less compared to that of the period of first 4 years (1993–1996). The mean seminal fluid volume in the first decade (1993–2002) had decreased by 11.4% compared to that of the last decade (2003–2012). Our data demonstrate a gradual decrease in the seminal fluid volume.

### Table 2: Distribution pattern of hypospermia, azoospermia, and oligozoospermia among the North Norwegian men from 1993 to 2012 who approached for the infertility treatment.

<table>
<thead>
<tr>
<th>Year</th>
<th>Average age (years)</th>
<th>Total subjects</th>
<th>Hypospermic population (%)</th>
<th>Azoospermic population (%)</th>
<th>Oligozoospermic population (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>32.0</td>
<td>281</td>
<td>24 (6.8)</td>
<td>12 (4.3)</td>
<td>56 (19.9)</td>
</tr>
<tr>
<td>1994</td>
<td>32.0</td>
<td>180</td>
<td>14 (4.5)</td>
<td>9 (5.0)</td>
<td>47 (26.1)</td>
</tr>
<tr>
<td>1995</td>
<td>33.0</td>
<td>212</td>
<td>26 (11.3)</td>
<td>16 (7.5)</td>
<td>56 (26.4)</td>
</tr>
<tr>
<td>1996</td>
<td>34.0</td>
<td>304</td>
<td>40 (12.8)</td>
<td>17 (5.6)</td>
<td>72 (23.7)</td>
</tr>
<tr>
<td>1997</td>
<td>33.8</td>
<td>360</td>
<td>47 (13.1)</td>
<td>21 (5.8)</td>
<td>96 (26.7)</td>
</tr>
<tr>
<td>1998</td>
<td>33.9</td>
<td>236</td>
<td>27 (11.0)</td>
<td>16 (6.8)</td>
<td>62 (26.3)</td>
</tr>
<tr>
<td>1999</td>
<td>33.5</td>
<td>288</td>
<td>34 (11.5)</td>
<td>17 (5.9)</td>
<td>97 (33.7)</td>
</tr>
<tr>
<td>2000</td>
<td>34.4</td>
<td>274</td>
<td>39 (11.7)</td>
<td>27 (9.9)</td>
<td>72 (26.3)</td>
</tr>
<tr>
<td>2001</td>
<td>34.6</td>
<td>389</td>
<td>52 (12.1)</td>
<td>18 (4.6)</td>
<td>108 (27.8)</td>
</tr>
<tr>
<td>2002</td>
<td>34.4</td>
<td>225</td>
<td>32 (14.2)</td>
<td>18 (8.0)</td>
<td>60 (26.7)</td>
</tr>
<tr>
<td>2003</td>
<td>34.7</td>
<td>286</td>
<td>41 (14.3)</td>
<td>18 (6.3)</td>
<td>90 (31.5)</td>
</tr>
<tr>
<td>2004</td>
<td>35.5</td>
<td>294</td>
<td>46 (15.7)</td>
<td>26 (8.8)</td>
<td>96 (32.7)</td>
</tr>
<tr>
<td>2005</td>
<td>35.3</td>
<td>297</td>
<td>45 (15.2)</td>
<td>47 (15.8)</td>
<td>82 (27.6)</td>
</tr>
<tr>
<td>2006</td>
<td>36.3</td>
<td>261</td>
<td>35 (13.5)</td>
<td>31 (11.9)</td>
<td>70 (26.8)</td>
</tr>
<tr>
<td>2007</td>
<td>35.6</td>
<td>274</td>
<td>35 (12.8)</td>
<td>40 (14.6)</td>
<td>74 (27.0)</td>
</tr>
<tr>
<td>2008</td>
<td>35.7</td>
<td>290</td>
<td>44 (15.0)</td>
<td>38 (13.1)</td>
<td>86 (29.7)</td>
</tr>
<tr>
<td>2009</td>
<td>35.2</td>
<td>323</td>
<td>47 (14.7)</td>
<td>54 (16.7)</td>
<td>95 (29.4)</td>
</tr>
<tr>
<td>2010</td>
<td>35.5</td>
<td>329</td>
<td>55 (16.8)</td>
<td>39 (11.9)</td>
<td>97 (29.5)</td>
</tr>
<tr>
<td>2011</td>
<td>35.6</td>
<td>303</td>
<td>52 (17.4)</td>
<td>53 (17.5)</td>
<td>82 (27.1)</td>
</tr>
<tr>
<td>2012</td>
<td>35.0</td>
<td>333</td>
<td>54 (16.5)</td>
<td>46 (13.8)</td>
<td>93 (27.9)</td>
</tr>
</tbody>
</table>

### Figure 2. Percentage of hypospermic population in North Norwegian men from 1993 to 2012. The bar represents the percentage of hypospermic males who attended to the hospital for infertility treatment on the particular year, as described in Table 1.

### Figure 3. Comparison of hypospermic, azoospermic and oligozoospermic North Norwegian men seeking infertility treatment from 1993 to 2012. The results are expressed as the percentage values and compared between the first decade (1993–2002, n = 2749) and the last decade (2003–2012, n = 2990).

The mean seminal fluid volume (2.9 ± 0.1 mL) in the periods of last 4 years (2009–2012) was 26.0% less compared to that of the period of first 4 years (1993–1996). The mean seminal fluid volume in the first decade (1993–2002) had decreased by 11.4% compared to that of the last decade (2003–2012). Our data demonstrate a gradual decrease in the seminal fluid volume.
among men seeking fertility treatment in Northern Norway over
the past 20 years (Table 1 and Figure 1).

Carlsen et al. reported a significant decrease in the sperm cell
count from $113 \times 10^6$ mL$^{-1}$ in 1940 to $66 \times 10^6$ mL$^{-1}$ in 1990
and the mean seminal fluid volume from 3.4 mL to 2.75 mL,
respectively (Carlsen et al., 1992). However, the data included
in the analysis were heterogeneous and included both healthy as
well as infertile men. Auger et al. reported the mean sperm cell
concentration of $89 \times 10^6$ mL$^{-1}$ in 1973 and $60 \times 10^6$ mL$^{-1}$ in
1992, indicating a decrease by 2.1% per year among healthy
sperm donors in Paris (8) who had fathered at least one child
previously. In our study among men seeking fertility treatment,
the mean sperm cell concentration and total sperm cell count in
the last decade (2003–2012) had decreased by 23.1% and 28.9%,
respectively, compared to that of the first decade (1993–2002).
However, it is interesting to note that the semen volume and
sperm cell concentration reported in the last period of the study
(1992) by Auger et al. (1995) were similar to the corresponding
data in the earlier period (1992) of our study. Furthermore, the
proportion of hypospermic men in our study population had
doubled in the last 20 years with the rate of 4.4% per year (Figure
2). Similar trends were also observed for the azoospermic and
oligozoospermic population (Figure 3). The results of our study
showed a similar temporal trend of deteriorating semen quality
as reported by others two decades ago (Auger et al., 1995; Carls-
sen et al., 1992) irrespective of the population studied.

As our study was performed in a self-selected population of
men seeking fertility treatment, the results may not be applica-
table to the general population. Additionally, as the mean age of
men seeking fertility treatment increased from 32.0 years to
35.6 years, it could be argued that the decreasing semen quality
is due to increasing age. However, regression analysis showed
that the patient’s age had no significant effect on the semen
quality. According to Kidd et al., decreases in the semen vol-
ume (3–22%), sperm cell motility (3–37%), and percent normal
spermatozoa (4–18%) are likely when comparing the 30-year-
old to 50-year-old men; however, the semen quality among the
male population aged 32 and 36 years is not significantly dif-
ferent (Kidd et al., 2001). Therefore, the change in the mean age
is unlikely to have contributed significantly to the semen profile
changes seen in our study.

Several studies have shown that the sperm cell motility,
more particularly the percentage of spermatozoa with ‘grade
3–4’ motility, is the strongest indicator of the potential in vivo
fertilizing capacity of semen (Comhaire et al., 1994). In the
fertility clinics, including ours, even the low-grade motility
sperm cell can be used to successfully fertilize an ovum using
intracytoplasmic sperm injection. However, the relationship
between pregnancy outcome and sperm motility remains incon-
cclusive. As sperm motility and morphology are evaluated sub-
jectively, these data are not presented in the present article.

Our study did not allow us to identify the possible cause(s) of
the observed deterioration in the semen quality. Cigarette
smoking has been found to be associated with a significant
decline in sperm cell concentration (−15.3%), total sperm cell
count (−17.5%), total number of motile sperm cells (−16.6%),
and citrate concentration (−22.4%) (Kunzle et al., 2003). We
did not have information on the lifestyle factors on these men,
but the changes in the lifestyle can hardly be held responsible
for deteriorating trend of semen quality, particularly since the
consumption of, for example, tobacco seems to have decreased
in the overall population (Bartecchi et al., 1994).

It can be speculated that environmental factors might
be responsible for the observed deterioration of semen charac-
teristics (Jensen et al., 1995; Sharpe and Skakkebæk, 1993;
Vanhoorne et al., 1994). Geoffroy-Siraudin et al. speculated
the decline of semen quality due to the heavy industrial
pollution in Marseille, France (Geoffroy-Siraudin et al.,
2012). In general, North Norway is considered to be a less
polluted region with no noticeable heavy industries. However,
the trend of changing semen profile observed in North Norway
appears to be similar to that in the big cities (Adamopoulos
et al., 1996; Auger et al., 1995; Geoffroy-Siraudin et al.,
2012; Irvine et al., 1996; Van Waeledhem et al., 1996; Younglai
et al., 1998). Therefore, it might be due to several other factors
rather than environmental pollution. It has been suggested that
the acute exposure to radiofrequency fields of cellular phones
may modulate the oxidative stress of free radicals by enhancing
lipid peroxidation and cause a decrease in the activity of the
antioxidants, superoxide dismutase, and glutathione peroxi-
dase, in human erythrocytes (Moustafa et al., 2001). In addition,
genotoxic effect on epididymal spermatozoa has been reported
when mice were irradiated 12 h per day by radiofrequency for
7 days (Aitken et al., 2005). Use of laptop computer connected
to Internet through Wi-Fi is also reported to decrease human
sperm cell motility and increase in DNA fragmentation by
enhancing oxidative stress (Avendano et al., 2012). However,
it should be noted that there are several reports showing
decreasing semen quality in 1940–1990 period (Auger et al.,
1995; Carlsen et al., 1992), and at that time, there were no
laptop computers or Wi-Fi. Therefore, there is no direct evi-
cence to claim that the use of computers and mobile phones
is responsible for the change in semen profile; however, a
closer evaluation may be worthwhile.

Population migration has significantly increased over the
last 20 years in North Norwegian region. Our analysis does not
distinguish indigenous population from immigrated one. There-
fore, the possibility of changes in semen profile due to the
demographic changes cannot be excluded. Moreover, present
results on semen analysis were taken from the men among
couples seeking infertility treatment and not from the healthy
population. Therefore, arguably the same trend of semen qual-
ity decline might not be observed in the healthy population.

Conclusion

In this study, we found that the semen quality of men among
couples seeking fertility treatment is progressively declining.
However, the causes of semen quality deterioration and its
effect on fertility potential remain to be elucidated. Further
studies are needed to clarify temporal trends in semen quality
in the general population of the Arctic region.
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