The experience of in vitro fertilization data collection in Turkey

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Abstract

Collecting and reporting data is a crucial aspect of in vitro fertilization (IVF) practice. During the following two decades after the first report of the European IVF-monitoring Consortium (EIM) on IVF data, the number of contributing countries increased gradually reaching nearly forty. For the first seven years of publication, between 2001 and 2007, Turkey did not provide IVF data to the European registry. Turkey first took part in the European registry in 2008 and thus also in the World registry. The addition of Turkish data to EIM was an important milestone, since Turkey appeared as the country with the sixth highest number of cycles, performing nearly eight percent of all European assisted reproductive technology (ART) cycles. Turkey continued contributing to the European registry for the following four years consecutively but after 2012 the input of Turkish IVF data stopped. Strikingly, between 2008-2012 Turkey became one of the main contributors to the registry with an ability to give a full report. So far, we do not have a complete European set of data and the number of cycles reported by European Society for Human Reproduction and Embryology (ESHRE) EIM can easily be said to be an underestimation of the actual number of cycles. IVF data from Turkey - a country having the 17th highest population in the World and appearing among the first six countries in Europe in terms of the number of ART cycles per year - will definitely contribute very much to ESHRE EIM database. It is now time to turn the tide and restart submitting Turkish data to European registry, but this time regularly and in a systematic method. Such an achievement will greatly contribute to the aim of EIM of achieving a complete data set. (J Turk Ger Gynecol Assoc 2021; 22: 235-41)

Keywords: IVF, assisted reproduction, data collection

Introduction

After the report of the first successful in vitro fertilization (IVF) treatment more than forty years ago (1), practitioners in the field focused on optimization of the laboratory set up and improving treatment protocols as the primary goals. This has resulted in a gradual evolution of the technique during the following four decades (2). As the technique started to be used more extensively in all geographical regions of the world, concerns about creating a database arose. Australia was the first country to establish a data registry in 1992. The initial regional data came from Australia-New Zealand (3), Latin America (4) and the USA and Canada (5). The first global data were presented at congresses in the early 1990s (6,7) and published as an article in 1997 (8). Recently China presented assisted reproductive technology (ART) data for the first time, showing that nearly one-third of all global cycles were performed in mainland China (9). Europe, a region performing roughly another one-third of all global ART treatments and with the largest number of ART cycles compared with the other regions of the World (10), started to contribute to the world registry a couple of years later (11). This delay of the European registry data compared to other regions is probably due to the difficulty of creating a consortium and collaborative work. Europe consists of many countries practising with heterogeneous dynamics in the continent and these countries have diverse cultural, political, economic and legal systems, often lacking national data registers dealing with reproduction. When we look back at the history of data collection process in Europe, this started with contact between the European Society...
for Human Reproduction and Embryology (ESHRE) and either national registers or key persons of all European countries in 1999. Initially eighteen countries responded and the first report was produced in 2001 pertaining to cycles performed in 1997 (11). In this first report, France appeared as the leading country regarding the total number of ART cycles, followed by the United Kingdom and Germany was third, with all three countries reporting >50% of all cycles. During the following two decades, the number of contributing countries increased gradually, reaching nearly forty with slight fluctuations in the number of countries reporting on a yearly basis (12,13). So far seventeen countries have been contributing to the registry regularly from the very beginning, with some countries joining after several years and continuing regularly and some others providing data irregularly for a few years either consecutively or separately (Figure 1, 2).

The first successful IVF treatment in Turkey was accomplished a decade after the birth of the world’s first IVF baby (14). During the following years, the number of IVF clinics, as well as the number of IVF cycles in the country increased steadily and rapidly. For the first seven years of the European IVF-monitoring Consortium (EIM) registry pertaining to the period 1997-2003, Turkey did not provide IVF data to the European registry. In 2005 Mete Işıkoğlu from Turkey contacted the chairman of the consortium, Karl Nygren, personally enquiring as to the reasons of failure to submit data and what the current situation was. Prof. Nygren kindly gave a prompt response with a suggestion of collaboration and sent his suggestions. After mutually checking all the probabilities for a feasible solution via e-mail, as a next step, Işıkoğlu brought the issue for discussion in the executive committee-meeting of Society of IVF Centers, Turkey (SICT-Formerly Society of Private IVF Centers) for which he was a delegate and is currently the president. After negotiations, upon the decision of SICT he was charged to lead the process and participated in the EIM meeting held in Lausanne in 2007 as the Turkish representative. Soon after this meeting, SICT invited all IVF centers in the country via e-mail and regular mail to submit their data voluntarily. In the end, four out of 78 IVF centers, each from four major cities (İstanbul, Ankara, İzmir, Antalya) provided their data. In 2008 for the first time, Turkey took part in the European registry, reporting data pertaining to 2004 (15) and, with its inclusion in the collective European data, in the World registry (16).

Starting the submission of Turkish data to EIM was an important milestone since Turkey carried out the sixth highest number of cycles, performing nearly eight percent of all European ART cycles (Table 1). Turkey continued contributing to the European registry for the following four years consecutively, through

Figure 1. Number of years regarding the contribution of each country in decreasing order between 1997-2016

Table 1. Percentage of cycles from Turkey in total over five years

| Year | #IVF Clinics in Turkey | Total cycles in Europe | Cycles reported from Turkey | Rank in row from the top | % of Turkish cycles in total |
|------|------------------------|------------------------|-----------------------------|--------------------------|-------------------------------|
|      | Total                  | Reporting              |                             |                          |                               |
| 2004 | 78                     | 4                      | 367066                      | 3575                     | 17*                           | 0.97*                         |
| 2005 | 93                     | 61                     | 418111                      | 28417                    | 6                             | 6.80                          |
| 2006 | 77                     | 77                     | 458759                      | 37468                    | 6                             | 8.17                          |
| 2007 | 92                     | 92                     | 493184                      | 35386                    | 6                             | 7.18                          |
| 2008 | 107                    | 107                    | 531260                      | 43928                    | 5                             | 8.27                          |

*Note the limited number of clinics reporting.

IVF: In vitro fertilization
the efforts of Timur Gurgan from the Society of Reproductive Medicine, Turkey. However, after 2012 the input of Turkish IVF data stopped again (17). Data on birth outcome and frozen embryo replacement cycles were not available. Strikingly, for the database pertaining to treatments between 2004-2008 Turkey became one of the main contributors to the registry with an ability to give a full report. When we take into consideration that nearly 5-7% of the cycles in Europe are egg donation treatments and that third party reproductive treatments are not allowed in Turkey, actual contribution of Turkish data to non-donor cycle pool of the European registry is probably higher.

The current situation

At the moment there are five regional registries in the World, namely ESHRE EIM, Society of Assisted Reproductive Technology, Australia and New Zealand Assisted Reproduction Database [formerly National Perinatal Epidemiology and Statistics Unit, since 2004 known as the Australia and New Zealand Assisted Reproduction Database (ANZARD)], Latin America and The African Network and Registry for Assisted Reproductive Technology. The Middle East Registry used to provide data but does not work regularly at the moment. The International Committee for Monitoring Assisted Reproductive Technology is the organization collecting worldwide data since 1989 (18) and reporting up-to-date data almost regularly every other year. To date, we do not have a complete European set of data and the number of cycles reported by ESHRE EIM is very probably an underestimation of the actual number of cycles. When the number of countries that have contributed so far (n=42) is multiplied by the number of years data published (n=20), it makes 840 country-years but the actual reported country-years so far (sum of the number of contributing countries of all years) is 603 which means that the available database so far represents nearly 71% of the performed cycles by the reporting clinics during the whole period. The fact that not all the clinics are reporting (roughly 82%) from every country is an additional weakness of the registry. Only seventeen countries have contributed to the registry regularly every single year from the beginning, while some others also provided data regularly albeit having joined the consortium several years later. Considering the last five years, six countries dominate by the number of cycles (France, Germany, Italy, UK, Russia, and Spain) constituting nearly two thirds of the grand total (13,19-23). Currently the only available data source in Turkey is the official records administered and kept by the relevant department of Government of Health (24) which annually collects IVF data pertaining to the previous year from all private and government based clinics. These data used to be collected as paper-work up to 2011 and online thereafter. The obvious advantage of this system is that the data is gathered regularly from all clinics since it is a compulsory reporting system. On the other hand, there are some potential shortcomings of this existing system which weaken the usefulness and reliability of the data quality. Firstly, since the data represents the previous year, all pregnancy variables and outcome cannot be obtained accurately (obstetric and neonatal outcome is not obtained from a national based birth registry, but is provided by the individual IVF clinics instead). Secondly, the data collecting authority is also the law maker and the inspector of the health care system. Furthermore data is not submitted in an anonymous or voluntary manner. Hence, the clinic directors may feel hesitancy to report some inadvertent events which may result in statistical bias, a fact more or less a universally valid probability for all national registries (25). Finally, this official registry is neither published anywhere nor is available as an open access to professionals or lay people. As the documentation of adverse events is a crucial part of an IVF registry, it is worth remembering the utmost importance of fundamentals i.e. surveillance and vigilance while collecting data which is valid in any field of medicine. Thus, even though data submission in a voluntary manner may theoretically overcome such a handicap in some countries, compulsory submission may work better in other societies.

Up to now, there has been no collaboration between the government authority and any of the national societies regarding data collection. Since there is no collaboration between the national authority and ESHRE either, the possibility of a regular data flow from the current Turkish database to ESHRE EIM registry seems quite low. From the very beginning of the negotiations regarding the issue of creating a national IVF data registry, special sessions have been held in almost all extended national IVF congresses. Strenuous efforts of the delegates of the national societies have not been able to achieve the initiation of a collaborative work between the national IVF societies and the national health authorities. Even so, trying to convince the national authorities may be an option to resume the submission of national IVF data to international database.

Future perspectives

In general, collecting data is important in many ways: instead of guessing what is going on, robust data allows the storage and analysis of important information about the existing situation and helps to plan for a potential future. An IVF database not only reveals the clinical pregnancy variables but also the side effects and the follow up of children’s health. Long term data also reveals the progress of IVF outcome variables, provides an available source of research and helps to inform patients who may have questions about the IVF process. Although the history of IVF dates back more than forty years ago, ESHRE EIM has
| 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 |
|------|------|------|------|------|------|------|------|------|------|------|
| Albania | - | - | - | - | - | - | - | 123 | 146 | 141 | 161 |
| Armenia | - | - | - | - | - | - | - | - | - | - | - |
| Austria | - | - | - | - | - | - | 887 | 880 | 1003 | 886 | 1387 | 1369 |
| Belarus | - | - | - | - | - | - | - | - | - | - | - |
| Belgium | 7552 | 10529 | 10511 | 11823 | 12205 | 12877 | 15594 | 19759 | 22012 | 22730 | 24459 |
| Bosnia* | - | - | - | - | - | - | - | - | - | - | 162 |
| Bulgaria | - | - | - | - | 396 | 877 | 880 | 1003 | 886 | 1387 | 1369 |
| Croatia | - | - | - | - | - | - | 2621 | 2707 | - | - | - |
| Cyprus | - | - | - | - | - | - | 1032 | - | - | - | 1432 | 1590 |
| Czech Republic | 7940 | 7943 | 8718 | 2605 | - | - | - | 5168 | 13707 | 15060 | - |
| Denmark | 7855 | 8530 | 8793 | 9682 | 10305 | 11321 | 10893 | 11518 | 11931 | 12618 | 14067 |
| Estonia | - | - | - | - | - | - | - | - | - | - | - |
| Finland | 7909 | 7877 | 7320 | 7489 | 7980 | 8352 | 7533 | 9204 | 8202 | 9116 | 8935 |
| France | 45687 | 46720 | 51868 | 56754 | 54626 | 59296 | 60681 | 69746 | 71278 | 65749 | 67572 |
| Germany | 27927 | 46132 | 60723 | 63005 | 71752 | 84819 | 102426 | 56813 | 53378 | 54995 | 62322 |
| Greece | 7277 | 7388 | 6776 | 5888 | 4063 | 5589 | 9790 | 9810 | 10110 | 3971 | 2503 |
| Hungary | 1747 | 2099 | 2024 | 2157 | 6277 | 6814 | 2850 | 2878 | 3563 | 3307 | 3128 |
| Iceland | 384 | 422 | 415 | 364 | 360 | 352 | 387 | 316 | 583 | 530 | 665 |
| Ireland | - | - | 1338 | 1570 | 1724 | 1912 | 2058 | 2580 | 2860 | 3232 | 3565 |
| Italy | 9570 | 13868 | 15316 | 19835 | 18602 | 18948 | 25877 | 26099 | 34541 | 40748 | 43708 |
| Kazakhstan | - | - | - | - | - | - | - | - | - | - | - |
| Latvia | - | - | - | 116 | - | 147 | 184 | - | 280 | 352 | - |
| Lithuania | - | - | - | - | - | 82 | 83 | 68 | 413 | 425 | - |
| Luxembourg | - | - | - | - | - | - | - | - | - | - | - |
| Macedonia** | - | - | - | - | - | 241 | 383 | 522 | 638 | 911 | 1008 |
| Malta | - | - | - | - | - | - | - | - | - | - | - |
| Moldova | - | - | - | - | - | - | - | - | - | - | - |
| Norway | 3562 | 3643 | 4029 | 4340 | 4396 | 4180 | 5314 | 6078 | 6672 | 7134 | 7871 |
| Poland | - | - | - | 3728 | 4262 | 4303 | 4163 | 5059 | 5962 | 6223 | 7515 |
| Portugal | 1183 | 1217 | 1760 | 2079 | 2208 | 2955 | 3108 | 2904 | 3806 | 3871 | 5236 |
| Romania | - | - | - | - | - | - | - | - | - | - | - |
| Russia | 3123 | 4692 | 4789 | 6363 | 7665 | 8667 | 10819 | 14872 | 17553 | 21274 | 26983 |
| Montenegro | - | - | - | - | - | - | 380 | 187 | 164 | 245 | 278 |
| Serbia | - | - | - | - | - | - | - | - | 250 | 526 | 1126 |
| Slovenia | - | - | - | 2374 | 2237 | 2576 | 2643 | 2725 | 2907 | 2807 | 3428 |
| Spain | 12603 | 9962 | 11616 | 14519 | 13355 | 15030 | 17011 | 40956 | 41689 | 49943 | 54620 |
| Sweden | 8424 | 8381 | 8660 | 9205 | 10082 | 11081 | 11736 | 12871 | 13647 | 14931 | 15061 |
| Switzerland | 3346 | 4002 | 4166 | 4644 | 4929 | 5385 | 5628 | 5718 | 6126 | 7109 | 7815 |
| The Netherlands | 13700 | 13965 | 14378 | 15062 | 15335 | 16273 | 17649 | 15366 | 17462 | 17770 | 19699 |
| Turkey | - | - | - | - | - | - | - | - | 3575 | 28417 | 37468 | 35386 |
| UK | 34398 | 35261 | 30215 | 34634 | 35492 | 37083 | 37348 | 39981 | 41768 | 43953 | 46688 |
| Ukraine | - | - | 914 | 1147 | 1487 | 1694 | 2132 | 1632 | 3517 | 5361 | 4899 |

Figure 2. Total number of ART cycles in European countries between 1997-2016.
*(Bosnia Herzegovina after 2013), **(North Macedonia in 2020)
|            | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 |
|------------|------|------|------|------|------|------|------|------|------|
| Albania    | 164  | -    | -    | -    | 289  | 139  | 153  | 178  | 175  |
| Armenia    | -    | -    | -    | -    | -    | -    | -    | 1465 | 346  |
| Austria    | 6540 | 6277 | 6402 | 6676 | 6822 | 7173 | 7326 | 8778 | 9721 |
| Belarus    | -    | -    | -    | 2216 | 2098 | 2451 | 2739 | 2969 | 2997 |
| Belgium    | 28751| 27674| 28521| 29130| 28578| 28854| 28845| 30300| 30929|
| Bosnia*    | 180  | -    | -    | -    | -    | -    | -    | 598  | 280  |
| Bulgaria   | 3297 | 1797 | 5030 | 2101 | 7162 | 5380 | 6314 | 9849 | 11009|
| Croatia    | -    | 4296 | -    | -    | 3413 | 4818 | 2115 | -    | -    |
| Cyprus     | 1421 | -    | -    | 2046 | -    | 1850 | 1739 | 1737 | 1727 |
| Czech Republic | 18607| 19431| 20020| 20319| 22716| 25318| 28759| 30107| 32543|
| Denmark    | 13476| 14992| 15954| 14560| 15142| 15143| 16167| 17454| 15917|
| Estonia    | 2259 | -    | -    | 2474 | 2715 | 2887 | 2884 | 2955 | 2952 |
| Finland    | 8997 | 8637 | 9312 | 9019 | 8824 | 8587 | 8642 | 9343 | 9191 |
| France     | 68446| 74475| 79427| 85253| 85594| 84214| 90434| 93918| 104773|
| Germany    | 69902| 67349| 62571| 67354| 71251| 76422| 81177| 96512| 99226 |
| Greece     | 2476 | 2310 | 3693 | 5185 | 8207 | 18278| 24120| 27149| 27976|
| Hungary    | 3197 | 7068 | 5562 | 4681 | 4874 | 6152 | 5626 | 6262 | 5608 |
| Iceland    | 700  | 806  | 824  | 741  | 733  | 789  | 706  | 739  | 644  |
| Ireland    | 3489 | 4065 | 4078 | 3042 | 2843 | 1566 | 1513 | -    | 706  |
| Italy      | 47829| 52032| 58860| 63777| 64197| 64446| 68896| 73405| 77559|
| Kazakhstan | 1465 | 1474 | 2276 | 3209 | 3143 | 4612 | 3937 | 5020 | 4460 |
| Latvia     | 340  | 762  | -    | -    | -    | 674  | 1390 | 2143 | 1528 |
| Lithuania  | 463  | 131  | 131  | 115  | 173  | 380  | 381  | 655  | 758  |
| Luxembourg | -    | -    | -    | -    | -    | -    | -    | -    | -    |
| Macedonia**| 1536 | 2065 | 1497 | -    | -    | 1699 | 1987 | 2136 | 2934 |
| Malta      | -    | -    | -    | -    | -    | 100  | 176  | 311  | 359  |
| Moldova    | 613  | 625  | 624  | 632  | 1187 | 966  | 843  | 993  | 934  |
| Norway     | 8535 | 8544 | 9007 | 8927 | 8982 | 8169 | 10925| 10324| 10280|
| Poland     | 10490| 12068| 13325| 15507| 16849| 20968| 23594| 26491| 31349|
| Portugal   | 5569 | 6077 | 7179 | 7107 | 7444 | 7362 | 7786 | 8660 | 9365 |
| Romania    | 1143 | 1052 | 1151 | 1553 | 1956 | 2444 | 3557 | 3935 | 5009 |
| Russia     | 31217| 42110| 34026| 57094| 62620| 67861| 94985| 110723| 121235|
| Montenegro | 370  | 482  | 452  | 445  | 540  | 475  | 442  | 506  | 566  |
| Serbia     | 1574 | 1232 | 1484 | 1560 | 1560 | 2064 | 2720 | 278  | 488  |
| Slovenia   | 3705 | 3680 | 4419 | 4069 | 4597 | 4755 | 4684 | 4649 | 4725 |
| Spain      | 38245| 54266| 58735| 68756| 69699| 78152| 109275| 119875| 140909|
| Sweden     | 16107| 16714| 17628| 18562| 18280| 18266| 18213| 18603| 18989|
| Switzerland| 8477 | 9099 | 9540 | 9456 | 9546 | 9554 | 9922 | 10038| 10960|
| The Netherlands | 21164| 22061| 23627| 24182| 25173| 24951| 25141| 26136| 27901|
| Turkey     | 43928| -    | -    | -    | -    | -    | -    | -    | -    |
| UK         | 50555| 54314| 57856| 60377| 60151| 61728| 63504| 65461| 68308|
| Ukraine    | 7454 | 8077 | 7085 | 9851 | 12282| 15968| 16983| 19264| 20411|
been collecting European IVF data for the last twenty years and so far has revealed data pertaining to these last 20 years. There are more than fifty countries on the European continent, some of which are small states without IVF clinics and some only partially located in Europe (26). During the twenty-year history of the EIM IVF registry, 40 of these countries submitted national data. Since the data reporting system shows diversity in all these countries, a uniform quality assurance protocol is still lacking. There are two main concerns regarding the achievement of an ideal registry: first, reaching the ultimate aim of gathering complete IVF data from all European countries in a regular pattern. Second, the reliability of the registry should be as high as possible. Although it is not easy to reach the ideal point in practice regarding these two issues, one should keep in mind the saying that I first heard from Prof. Dr. Carl Nygren which I like and use frequently “little data is better than no data”. In order to be able to improve something one should certainly have a draft at hand.

EIM recently analysed the achievements and potential deficiencies in the twenty year registration process comparatively with registries from two other regions. They aimed to identify similarities and discrepancies between these registries in order to further improve data recording and interpretation. When the ESHRE/EIM registry is compared to the register of the Centres for Disease Control and Prevention and ANZARD, it was found that adverse events, such as maternal death, ovarian hyperstimulation syndrome and infections, were recorded sporadically and only by EIM and ANZARD. Although improvements are recorded in the three regional registers over time, inconsistencies and inaccuracies still remain and need to be identified. This reality necessitates the use of some caution when analyzing the data. EIM also defines an ultimate target of a continuous recording system, rather than the existing cross-sectional one, to achieve greater accuracy, independent of time span and borders (25).

Conclusion

The IVF data from Turkey - a country having the seventeenth highest population in the World and appearing among the first six countries in Europe in terms of the number of ART cycles per year- will definitely contribute greatly to the ESHRE EIM database. Then, it is time to turn the tide and restart submitting our data to the European registry, but this time regularly and in a systematic manner. In order to achieve this aim, a two-step approach would be simple and effective in solving the problem: the first step is the collaboration of the national IVF societies for a joint effort and construction of a national working group on data collection. There are four existing national societies in the field, one of which is the Society of Clinical Embryologists while the other three are general IVF societies, namely Society of Reproductive Health and Infertility (Üreme Sağlığı ve Infertilite Derneği), Society of Reproductive Medicine (Üreme Tıbbı ve Cerrahisi Derneği) and Society of IVF Centers (Tüp Bebek Merkezleri Derneği). One representative from each society is sufficient to accomplish this task. The next step should be simply inviting all clinics to submit data in a voluntary reporting system. Collecting the data in accordance with the datasets used by EIM will overcome the shortcoming of inability to provide data, such as for delivery outcome and frozen embryo replacement cycles. Such an achievement will greatly contribute to the aim of EIM of achieving a complete European data set.

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