

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

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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 heterogenous 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



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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, SCIT 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

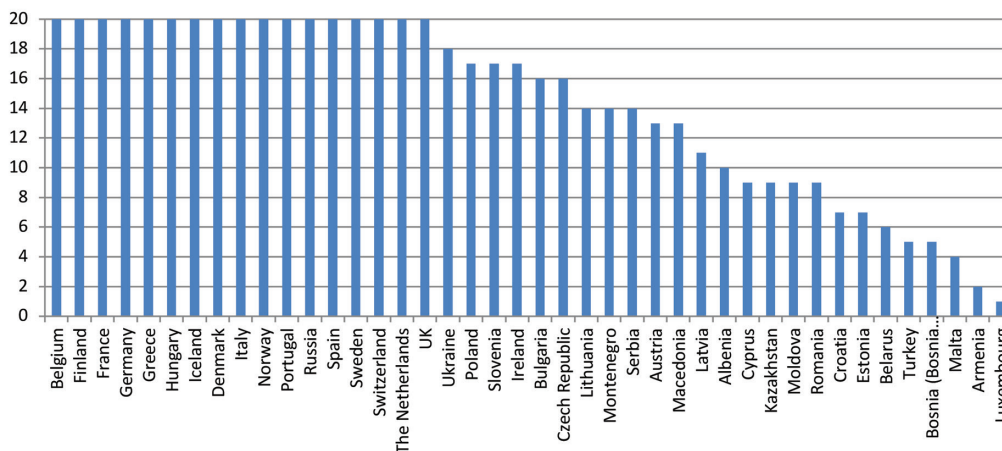


Figure 1. Number of years regarding the contribution of each country in decreasing order between 1997-2016

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	-	-	-	-	-	-	4887	4504	-	5177	5528
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	-	2807	-	-
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	45697	46720	51868	56754	54462	59296	60681	69746	71278	65749	67572
Germany	27927	46132	60723	63005	71752	84819	102426	56813	53378	54695	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	13680	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	5395	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	135
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									980
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	3357	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	2064	2720	278	488	286
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 İnfertilite 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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