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The Italian registry of therapeutic apheresis enters the information system of transfusion services - SISTRA

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ABSTRACT

The National Blood Centre (NBC) at the request of the Italian Scientific Society of Haemapheresis and Cell Manipulation (SIdEM) has funded and developed a software dedicated to the collection of data related to therapeutic apheresis procedures, known as the Italian Registry of Therapeutic Apheresis (IRTA). Although on a voluntary basis, participation in the registry was widespread. The data collected includes type and number of procedures, patients treated and their outcomes, and reported adverse events to the procedures.

For the years 2019 and 2020, the therapeutic apheresis procedure was widely used in the field of haematology, transplantation and rheumatology and was mainly associated with mild adverse events, thus showing a high level of safety. In addition to allowing the competent institution to monitor an important activity in the transfusion medicine field, the Registry is a new starting point for collaboration between transfusion centres distributed throughout the national territory and could encourage the design of major clinical trials.

1. Introduction

The Italian Registry of Therapeutic Apheresis (IRTA) has been active since 1999, thanks to the commitment of the SIdEM. The last IRTA was published in 2017 [1,2]. The Registry has been useful in performing specific studies as well as monitoring the adherence of the Apheresis Centres to the international guidelines for the clinical use of therapeutic apheresis procedures [3]. However, a dynamic and easy-to-use data management requires large investments, especially for updating the software, as also emerged during the World Apheresis Congress, held in Paris in 2016 [4,5]. Furthermore, therapeutic apheresis falls within the competence of transfusion medicine and 80 % of all procedures are carried out within Transfusion Services (TS) [6].

SISTRA is the Information System of the TS, developed as a strategic support for the achievement of the objectives established by the Italian law regulating blood transfusion. It is managed by the National Blood Centre (NBC) and uses the infrastructure of the Ministry of Health [7]. The system contains the registry of transfusion facilities and three categories of data are collected: data relating to transfusion activities, haemovigilance data and data on the transfer and acquisition of blood components and plasma derivatives produced from plasma needed to meet the clinical needs of Italy, region by region. The management and development of SISTRA is carried out by a team of NBC professionals.

Every Italian TS that is registered in the system can access SISTRA. For these reasons, SIdEM considered that SISTRA could also be the right support for therapeutic apheresis and asked the NBC to insert the Therapeutic Apheresis Registry project in SISTRA. Following the SIdEM's request for collaboration, the NBC developed and implemented the "*National Registry of Therapeutic Apheresis* " project within the TS information system. In this study we report the results of the first two years of activity of the National Registry of Therapeutic Apheresis using SISTRA.

2. Material and methods

The data collection software was presented in December 2019 to the SISTRA representatives from all over Italy in the conference dedicated to them that is organized every year. The NBC entrusted the presentation of the software's features and methods of use to the scientific society SIdEM.

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Table 1
Therapeutic apheresis procedures and number of patients treated (including paediatric patients) and emergency procedures.

Therapeutic procedure	N. Procedures (including emergency procedures)			N. Patients (including paediatric patients)			N. Paediatric patients			N. Emergency procedures		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
1 - Plasma exchange	11458	11272	−1.6	1942	1871	−3.7	24	31	29.2	666	782	17.4
2 - Cascade filtration	484	600	24.0	78	77	−1.3	0	0		4	2	−50.0
3 - Plasma adsorption (physical, chemical)	0	0		0	0		0	0		0	0	
4 - IgG / IgE Immunoadsorption	235	138	−41.3	20	18	−10.0	0	1		0	3	
5 - Photopheresis (online)	1624	2774	70.8	84	147	75.0	0	0		5	0	−100.0
6 - Photopheresis (off line)	2921	4776	63.5	235	475	102.1	17	19	11.8	8	5	−37.5
7 - Lipoprotein apheresis	377	441	17.0	38	42	10.5	3	4	33.3	0	0	
8 - Lymphoplasmapheresis	16	0	−100.0	7	0	−100.0	0	0		0	0	
9 - Cytoreductive leukapheresis	199	75	−62.3	170	43	−74.7	1	3	200.0	17	29	70.6
10 - Granulocyte-monocyto-apheresis	342	255	−25.4	48	33	−31.3	0	0		0	0	
11 - Therapeutic platelet apheresis	12	30	150.0	9	11	22.2	0	0		3	0	−100.0
12 - Erythrocyte exchange	1274	2110	65.6	231	366	58.4	58	53	−8.6	70	58	−17.1
13 - Erythroapheresis	2457	2787	13.4	827	988	19.5	9	5	−44.4	21	20	−4.8
14 - Stem Cell Collection (autotransplant)	2192	3236	47.6	1546	2197	42.1	58	118	103.4	49	85	73.5
15 - Other:	66	56	−15.2	18	53	194.4	2	3	50.0	1	0	−100.0
Total	**23657**	**28550**	**20.7**	**5253**	**6321**	**20.3**	**172**	**237**	**37.8**	**844**	**984**	**16.6**

The data collection software was created in an section of SISTRA called "*National Registry of Therapeutic Apheresis*". The types of procedures and diseases are identified by a code generated "ad hoc" within SISTRA.

Participation in the survey was voluntary and participants were asked to enter data for the years 2019 and 2020. The data collection was modelled on previous registries to facilitate data entry. Information relating to the census of the Therapeutic Apheresis Centres (TAC) - number and type of procedures performed, diseases treated, outcome of patients, and adverse events to apheresis procedures – was entered in this section.

In this paper, it was decided to present the data regarding the activity itself, and all the data received, even if incomplete, were analysed by descriptive analysis. However, no suitable assessment was made based on the four categories envisaged by the international guidelines. The data analysed are those present in SISTRA on June 14, 2021.

3. Results

In SISTRA 144 TACs registered and 93 (65 %) of them entered their data. The centres that participated in this first survey represent 81 % (17/21) of the Italian regions. The number of registered centres is in line with expectations. In 2019, 23657 procedures were carried, and this number increased to 28550 (+ 21 %) in 2020. Paediatric patients treated and emergency procedures rose by 38 % and 17 % respectively. Plasma exchange procedures were the most frequent, accounting for 48 % of the total in 2019 and 39 % in 2020. A 2% drop in plasma exchange was observed in 2020 compared to 2019, corresponding to a 4% drop in the number of patients treated. Offline photopheresis accounted for 12 % of total procedures in 2019 and 17 % in 2020 with an increase of 64 %. Adult patients increased by 102 % whereas paediatric patients by 12 %. Emergency procedures performed accounted for only 3.6 % in 2019 and 3.4 % in 2020 of the total. Erythropheresis accounted for approximately 10 % of all procedures in both years, and increased by 13 % in 2020 compared to 2019.The total number of patients treated increased by 21 % (Table 1).

The most numerous adverse events reported were mild reactions related to autologous hematopoietic stem cell (HSC) collections for autotransplantation. These events occurred in 14 % of the total procedures carried out in 2019 and 7% in 2020. Overall, complications in the two-year study period are comparable (1181 vs. 1172), with a distribution that saw an increase in events of moderate severity and a reduction in milder events: there was a clear drop in the most severe/serious, which in 2020 accounted for only 0.7 % of all adverse events. Plasma exchange (PEX) and peripheral stem cell harvesting were the procedures with the highest number of adverse events, but the majority were mild to moderate (PEX 98.5 %, 100 % HSC in 2020): no severe/serious events occurred in 2020 during the collection of HSCs (Table 2).

Table 3 describes the number of procedures of leucocyte/erythrocyte apheresis registered and the number of patients treated in 2019 and

Table 2
Adverse events to Therapeutic Procedures.

Therapeutic procedure	Mild			Moderate			Severe		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
1 - Plasma exchange	452	440	−2.7	61	84	37.7	15	8	−46.7
2 - Cascade filtration	30	7	−76.7	2	1	−50.0	1	0	−100.0
3 - Plasma adsorption (physical, chemical)	0	0		0	0		0	0	
4 - IgG / IgE Immunoadsorption	0	1		0	0		0	0	
5 - Photopheresis (online)	22	28	27.3	0	6		0	0	
6 - Photopheresis (off line)	123	157	27.6	2	3	50.0	0	0	
7 - Lipoprotein apheresis	0	11		0	1		0	0	
8 - Lymphoplasmapheresis	0	0		0	0		0	0	
9 - Cytoreductive leukapheresis	1	3	200.0	0	0		0	0	
10 - Granulocyte-monocytapheresis	50	50	0.0	0	0		0	0	
11 - Therapeutic platelet apheresis	0	0		0	0		0	0	
12 - Erythrocyte exchange	19	25	31.6	2	1	−50.0	0	0	
13 – Erythroapheresis	16	16	0.0	0	0		0	0	
14 – Haematopoietic Stem Cell Collection (HSCC- autotransplant)	314	237	−24.5	9	102	1,033.3	1	0	−100.0
15 - Other:	0	0		0	0		0	0	
Total	**1027**	**975**	**−5.1**	**76**	**198**	**160.5**	**17**	**8**	**−52.9**

Table 3
Haematopoietic Stem Cell collection (HSCC), Cytapheresis and Photopheresis: number of procedures and number of patients.

HSC Collection	N. Procedures			N. Patients		
	2019	2020	Δ%	2019	2020	Δ%
700 - Multiple myeloma	1158	1417	22.4	747	944	26.4
701 - Lymphoma	684	1155	68.9	545	896	64.4
702 - Acute leukaemia (Autograft / Back up)	161	258	60.2	124	155	25.0
703 - Neuroblastoma	23	62	169.6	17	42	147.1
704 - Other solid tumour	80	166	107.5	53	108	103.8
799 - Other:	31	33	6.5	24	29	20.8
Total	**2137**	**3091**	**44.6**	**1510**	**2174**	**44.0**
Cytapheresis	**2019**	**2020**	**Δ%**	**2019**	**2020**	**Δ%**
710 - Sickle Cell Disease (Erythrocyte Exchange)	1151	1616	40.4	193	272	40.9
711 - Malaria (Erythrocyte Exchange)	0	0		0	0	
712 - Polycythaemia / Erythrocytosis (Erythroapheresis)	482	1990	312.9	250	586	134.4
713 - LAM (cytoreductive leukapheresis)	29	43	48.3	22	26	18.2
714 - ALL (cytoreductive leukapheresis)	15	22	46.7	10	11	10.0
799 - Other:	29	83	186.2	9	20	122.2
Total	**1706**	**3754**	**120.0**	**484**	**915**	**89.0**
Photopheresis	**2019**	**2020**	**Δ%**	**2019**	**2020**	**Δ%**
720 - GvHD	3310	4907	48.2	213	309	45.1
721 - Rejection of solid organ	333	910	173.3	20	53	165.0
722 - Cutaneous T lymphoma / Sezary syndrome	663	952	43.6	48	70	45.8
723 - Autoimmune diseases	109	86	−21.1	2	7	250.0
799 - Other:	0	8		0	1	
Total	**4415**	**6863**	**55.4**	**283**	**440**	**55.5**

2020. Collection of stem cells, erythrocytapheresis, and photopheresis increased in 2020, as well as the number of patients treated: in particular, there was an increase of the collection of HSCs in multiple myeloma (+ 22 %), in lymphoma (+69 %) and in acute leukaemia (+60 %). Erythrocytapheresis in polycythaemia increased by 313 %, and by 134 % for the related patients.

Erythrocyte exchange procedures for the treatment of sickle cell anaemia also increased in 2020, with a 40 % and a 41 % rise in the number of procedures and patients respectively. Compared to 2019, photopheresis figures increased by 55 % in 2020 for both the number of procedures and patients. The following tables show the pathologies treated with therapeutic apheresis procedures divided by specialist branch with the patient outcome. As the survey in this first edition of the registry using SISTRA was voluntary, in many cases patient outcomes were not reported.

Table 4 shows the neurological pathologies among which Myasthenia gravis accounted for 48 % of all the specified pathologies in 2019 and 47 % in 2020. Patients treated in both years accounted for 42 % of the total.

The outcome of patients treated for myasthenia gravis was specified in 79 % of cases in 2019 and 83 % in 2020. In both years 10 % of patients recovered, 80 % improved in 2019 and 75 % in 2020, 9% in 2019 and 13 % in 2020 remained unchanged, and 2% in 2019 and 1% in 2020 worsened (Table 5).

As shown in Table 6, of the haematological pathologies taken into consideration, Polycythaemia vera-Erythrocytosis was the most treated. In 2019 it accounted for 31 % and in 2020 25 % of the procedures carried out in blood diseases.

Patients undergoing this treatment accounted for 53 % of the total in 2019 and 43 % in 2020.The outcome of patients with Polycythaemia vera-Erythrocytosis treated overall was indicated in 53 % of cases in 2019 and in 41 % in 2020 (Table 7).

TTP is also well represented, with 160 patients in 2020, undergoing 1350 procedures: it should be noted that in 2020 compared to 2019 the number of procedures/patient went from 11 to 8. This data could mean earlier intervention with drugs such as rituximab in the event of non-response to plasma exchange. The number of treatments in GvHD patients increased significantly in 2020, with procedures/ patient increasing from 14 in 2019 to 30 in 2020. In both 2019 and 2020, the outcome was indicated in too few cases, so as the results were not significant effectiveness could not be assessed.

In the rheumatology field, the disease for which therapeutic apheresis was used most was scleroderma. In 2020, however, despite the expected increase in the number of registered procedures, we saw a decrease. A possible explanation may be the reduction of outpatient activity in 2020 due to the COVID pandemic (Table 8).

In fact, apheresis in this pathology is always planned and never performed as an emergency procedure. The reorganization of the activities that took place in 2020 probably penalised the access of patients with slow-evolving chronic diseases such as scleroderma in most of the cases. Also in this clinical setting, no comment on the response to

Table 4
Neurological pathologies: number of procedures, number patients treated and number of patients at first diagnosis.

NEUROLOGY	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
1 - Acute disseminated encephalomyelitis (ADEM)	118	70	−41	22	15	−32	9	7	−22
2 - CIDP - Chronic inflammatory demyelinating polyneuropathy	1269	1260	−1	165	147	−11	39	34	−13
3 - Chronic focal Rasmussen encephalitis	6	0	−100	1	0	−100	1	0	−100
4 - Guillain-Barré syndrome	657	634	−4	137	124	−9	82	80	−2
5 - Complex regional pain syndrome	0	0		0	0		0	0	
6 - Lambert-Eaton syndrome	7	9	29	1	1	0	1	0	−100
7 - Multiple Sclerosis	378	305	−19	61	55	−10	23	18	−22
8 - Myasthenia Gravis	2930	2754	−6	371	350	−6	88	95	8
9 - Neuromyelitis optica	209	230	10	38	39	3	19	19	0
10 - NMDAR- antibodies encephalitis	28	80	186	5	12	140	1	9	800
11 - Paraneoplastic neurological syndromes	30	50	67	7	11	57	7	8	14
12 - Paraproteinemic demyelinating neuropathies	100	117	17	14	21	50	3	10	233
13 - PANDAS, Paediatric Autoimmune Neuropsychiatric Disorders Associated to Post-Streptococcal infection Syndrome	5	13	160	2	3	50	2	2	0
14 - Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	0	1		0	1		0	1	
15 - VG-potassium channel (VGKC) antibody related Diseases	1	7	600	1	1	0	0	0	
16 - Stiff person syndrome	132	65	−51	14	10	−29	1	2	100
991 - Other:	228	314	38	40	43	8	15	19	27
Total	**6098**	**5909**	**−3**	**879**	**833**	**−5**	**291**	**304**	**4**

Table 5
Neurological pathologies: outcome of patients.

NEUROLOGY	Patient Outcome											
	Remission			Improved			Unchanged			Worsened		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
1 - Acute disseminated encephalitis	0	0		9	8	−11.1	9	2	−77.8	0	1	
2 - CIDP - Chronic inflammatory demyelinated polyneuropathy	6	8	33.3	95	87	−8.4	32	33	3.1	2	5	150
3 - Chronic focal Rasmussen encephalitis	0	0		0	0		1	0	−100.0	0	0	
4 - Guillain-Barré syndrome	50	39	−22.0	46	49	6.5	9	9	0.0	2	5	150
5 - Complex regional pain syndrome	0	0		0	0		0	0		0	0	
6 - Lambert-Eaton syndrome	0	0		0	1		1	0	−100.0	0	0	
7 - Multiple Sclerosis	3	0	−100.0	33	31	−6.1	18	7	−61.1	0	1	
8 - Myasthenia Gravis	28	30	7.1	235	217	−7.7	26	39	50.0	5	3	−40
9 - Neuromyelitis optica	4	5	25.0	18	20	11.1	6	6	0.0	1	0	−100
10 - NMDAR- antibodies encephalitis	1	1	0.0	2	5	150.0	0	2		1	0	−100
11 - Paraneoplastic neurological syndromes	1	1	0.0	3	5	66.7	1	4	300.0	2	0	−100
12 - Paraproteinemic demyelinating neuropathies	0	2		12	5	−58.3	2	4	100.0	0	0	
13 - PANDAS, Paediatric Neuropsychiatric Post-Streptococcal Syndrome	0	0		2	2	0.0	0	1		0	0	
14 - Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	0	0		0	1		0	0		0	0	
15 - VG-potassium channel (VGKC) antibody related Diseases	0	0		0	0		0	0		0	0	
16 - Stiff person syndrome	0	0		5	6	20.0	8	3	−62.5	0	0	
991 - Other:	1	0	−100.0	26	19	−26.9	8	15	87.5	0	2	
Total	**94**	**86**	**−8.5**	**486**	**456**	**-6.2**	**121**	**125**	**3.3**	**13**	**17**	**31**

Table 6
Haematological disorders: number of procedures, number of patients treated and number of patients at first diagnosis.

HAEMATOLOGY	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
17 - Systemic amyloidosis	0	6		0	4		0	2	
18 - Autoimmune haemolytic anaemia-Cold agglutinin disease	7	11	57.1	2	3	50.0	1	3	200.0
19 - Coagulation factors inhibitors	1	14	1300.0	1	1	0.0	1	1	0.0
20 - Myeloma - acute renal failure	74	31	−58.1	21	10	−52.4	9	5	−44.4
21 - GVHD-Graft versus Host Disease	1492	3087	106.9	103	202	96.1	20	97	385.0
22 - ABO-incompatible haematopoietic stem cell transplantation	29	62	113.8	14	29	107.1	5	12	140.0
23 - Transplantation-haematopoietic stem cells, anti-HLA antibodies	3	24	700.0	1	10	900.0	0	7	
24 - Haemophagocytic syndromes	17	22	29.4	3	4	33.3	3	3	0.0
25 - Thrombocytopaenia / thrombosis induced by heparin	0	0		0	0		0	0	
26 - Immunological thrombocytopaenias	8	0	−100.0	3	0	−100.0	3	0	−100.0
27 - Hyperviscosity in hipergammaglobulinaemia	70	114	62.9	23	41	78.3	14	21	50.0
28 - Immunological thrombocytopaenia	0	0		0	0		0	0	
29 - Polycythaemia vera-Erythrocytosis	1972	2225	12.8	620	674	8.7	146	96	−34.2
30 - Post-transfusion purpura	0	0		0	0		0	0	
31 - Red Cell Immunization, D-antigen-Prevention and treatment	0	0		0	0		0	0	
32 - Anti-D immunization in pregnancy	0	34		0	3		0	2	
33 - Acute Sickle Cell Disease	212	150	−29.2	52	68	30.8	20	25	25.0
34 - Sickle Cell Disease, non-Acute Sickle Cell Disease	811	1441	77.7	130	228	75.4	13	12	−7.7
35 - Thrombocytosis	10	21	110.0	8	10	25.0	2	5	150.0
36 - Thrombotic, coagulation-mediated microangiopathy	24	42	75.0	4	7	75.0	0	1	
37 - Thrombotic, complement-mediated microangiopathy	33	13	−60.6	4	4	0.0	1	4	300.0
38 - Thrombotic microangiopathy associated with drugs	0	0		0	0		0	0	
39 - Thrombotic microangiopathy associated with infection	9	13	44.4	3	3	0.0	3	3	0.0
40 - Post-TMO thrombotic microangiopathy	1	50	4900.0	1	5	400.0	0	5	
41 - Thrombotic thrombocytopaenia purpura, TTP	1406	1350	−4.0	123	160	30.1	59	70	18.6
42 - Malaria	0	0		0	0		0	0	
43 - Babesiosi	0	0		0	0		0	0	
44 - Erythropoietic porphyria	7	10	42.9	1	1	0.0	0	0	
45 - Hereditary haemochromatosis	107	208	94.4	29	70	141.4	5	17	240.0
992 - Other:	75	52	−30.7	18	17	−5.6	6	13	116.7
Total	**6368**	**8980**	**41.0**	**1164**	**1554**	**33.5**	**311**	**404**	**29.9**

aphaeretic therapy is possible (Table 9).

In the field of nephrology, we analysed focal segmental glomerulosclerosis, which accounted for 58 % of the aphaeretic procedures performed in 2019 and 57 % in 2020 (Table 10).

The outcome of treated patients reported in the registry (31 % of total cases) showed that 1 patient in 2020 recovered and 1 worsened (5%), 58 % in 2019 and 74 % in 2020 improved, and 25 % in 2019 and 16 % in 2020 remained unchanged (Table 11).

In the dermatological field we analysed cutaneous T-cell lymphoma (Sézary syndrome) which was the pathology that both in 2019 (63 %) and in 2020 (79 %) represented the largest number of procedures performed (Table 12).

Among the gastrointestinal disorders, we analysed only chronic inflammatory bowel disease, which accounted for 83 % of procedures in 2019 and 50 % in 2020 with a decrease of 32 % (Table 13).

In the field of metabolic disorders, 60 % of the therapeutic apheresis procedures were carried out for familial hypercholesterolemia in 2019 and 56 % in 2020 of the total, and the number of patients treated

Table 7
Haematological disorders: outcome of patients.

HAEMATOLOGY	Patient Outcome											
	Remission			Improved			Unchanged			Worsened		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
17 - Systemic amyloidosis	0	0		0	2		0	2		0	0	
18 - Autoimmune haemolytic anaemia-Cold agglutinin disease	1	0	−100.0	0	2		1	0	−100.0	0	1	
19 - Coagulation factors inhibitors	0	0		1	1	0.0	0	0		0	0	
20 - Myeloma - acute renal failure	4	0	−100.0	14	6	−57.1	3	1	−66.7	0	0	
21 - GVHD-Graft versus Host Disease	5	34	580.0	66	87	31.8	1	15	1,400.0	2	11	450.0
22 - ABO-incompatible haematopoietic stem cell transplantation	2	0	−100.0	3	14	366.7	0	0		0	3	
23 - Transplantation-haematopoietic stem cells, anti-HLA antibodies	0	1		1	7	600.0	0	0		0	0	
24 - Haemophagocytic syndromes	1	0	−100.0	1	0	−100.0	0	1		1	3	200.0
25 - Thrombocytopaenia / thrombosis induced by heparin	0	0		0	0		0	0		0	0	
26 - Immunological thrombocytopaenias	2	0	−100.0	0	0		1	0	−100.0	0	0	
27 - hipergammaglobulinaemia	0	10		17	22	29.4	5	2	−60.0	0	4	
28 - Immunological thrombocytopaenia	0	0		0	0		0	0		0	0	
29 - Polycythaemia vera-Erythrocytosis	1	27	2,600.0	514	428	−16.7	0	12		0	0	
30 - Post-transfusion purpura	0	0		0	0		0	0		0	0	
31 - Red Cell Immunization, D-antigen-Prevention and treatment	0	0		0	0		0	0		0	0	
32 - Anti-D immunization in pregnancy	0	3		0	0		0	0		0	0	
33 - Acute Sickle Cell Disease	29	20	−31.0	17	40	135.3	0	0		0	0	
34 - Sickle Cell Disease, non-Acute Sickle Cell Disease	17	42	147.1	106	133	25.5	5	7	40.0	0	0	
35 - Thrombocytosis	0	0		3	6	100.0	1	1	0.0	0	0	
36 - Thrombotic, coagulation-mediated microangiopathy	2	5	150.0	1	1	0.0	1	0	−100.0	0	0	
37 - Thrombotic, complement-mediated microangiopathy	0	1		3	1	−66.7	1	2	100.0	0	0	
38 - Thrombotic microangiopathy associated with drugs	0	0		0	0		0	0		0	0	
39 - Thrombotic microangiopathy associated with infection	0	0		3	1	−66.7	0	1		0	1	
40 - Post-TMO thrombotic microangiopathy	0	1		0	2		1	0	−100.0	0	2	
41 - Thrombotic thrombocytopaenia purpura, TTP	82	91	11.0	9	26	188.9	3	6	100.0	8	4	−50.0
42 - Malaria	0	0		0	0		0	0		0	0	
43 - Babesiosi	0	0		0	0		0	0		0	0	
44 - Erythropoietic porphyria	0	0		1	1	0.0	0	0		0	0	
45 - Hereditary haemochromatosis	0	1		22	37	68.2	0	0		0	0	
992 - Other:	1	0	−100.0	10	8	−20.0	6	2	−66.7	0	1	
Total	**147**	**236**	**60.5**	**792**	**825**	**4.2**	**29**	**52**	**79.3**	**11**	**30**	**172.7**

Table 8
Rheumatological pathologies: number of procedures, number of patients treated and number of patients at first diagnosis.

RHEUMATOLOGY	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
46 - ANCA-associated glomerulonephritis	189	145	−23.3	38	28	−26.3	35	20	−42.9
48 - Cryoglobulinemia	211	280	32.7	20	28	400	3	5	66.7
49 - Schonlein-Henoch purpura	0	0		0	0		0	0	
50 - Vasculitis	186	231	24.2	26	37	423	13	17	30.8
51 - Cardiac neonatal lupus	6	0	−100.0	2	0	−100.0	2	0	−100.0
52 - Catastrophic Antiphospholipid-Acid Syndrome	55	40	−27.3	4	7	750	1	3	200.0
53 - Scleroderma	414	261	−37.0	23	19	−17.4	4	2	−50.0
54 - Systemic lupus erythematosus	63	65	3,2	11	12	9.1	7	9	28.6
994 - Other:	114	157	37.7	15	14	−6.7	10	7	−30.0
Total	**1238**	**1179**	**−4.8**	**139**	**145**	**4.3**	**75**	**63**	**−16.0**

Table 9
Rheumatological pathologies: outcome of patients.

RHEUMATOLOGY	Patient Outcome											
	Remission			Improved			Unchanged			Worsened		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
46 - ANCA-associated glomerulonephritis	5	1	−80.0	25	15	−40.0	8	6	−25.0	0	1	
48 - Cryoglobulinemia	2	2	0.0	11	21	90.9	4	4	0.0	1	0	−100.0
49 - Schonlein-Henoch purpura	0	0		0	0		0	0		0	0	
50 - Vasculitis	1	5	400.0	19	23	21.1	3	3	0.0	0	4	
51 - Cardiac neonatal lupus	0	0		0	0		2	0	−100.0	0	0	
52 - Catastrophic Antiphospholipid-Acid Syndrome	0	1		3	2	−33.3	0	2		0	1	
53 - Scleroderma	0	5		17	4	−76.5	4	9	125.0	0	1	
54 - Systemic lupus erythematosus	0	1		7	5	−28.6	4	5	25.0	0	1	
994 - Other:	0	2		12	8	−33.3	0	2		3	1	−66.7
Total	**8**	**17**	**112.5**	**94**	**78**	**−17.0**	**25**	**31**	**24.0**	**4**	**9**	**125.0**

Table 10
Nephrological pathologies: number of procedures, number of patients treated and number of patients at first diagnosis.

NEPHROLOGY	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
47 - Goodpasture Syndrome	53	91	71.7	8	9	12.5	2	7	250.0
56 - Focal Segmental GlomeruloSclerosis (FSGS)	184	214	16.3	12	19	58.3	8	6	−25.0
57 - IgA nephropathy	0	7		0	2		0	2	
58 - Nephrogenic systemic fibrosis	0	0		0	0		0	0	
995 - Other:	81	61	−24.7	16	14	−12.5	5	10	100.0
Total	**318**	**373**	**17.3**	**36**	**44**	**22.2**	**15**	**25**	**66.7**

Table 11
Nephrological pathologies: outcome of patients.

NEPHROLOGY	Patient Outcome											
	Remission			Improved			Unchanged			Worsened		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
47 - Goodpasture Syndrome	0	0		4	4	0.0	0	0		0	4	
56 - Focal segmental glomerulosclerosis	0	1		7	14	100.0	5	3	−40.0	0	1	
57 - IgA nephropathy	0	0		0	0		0	2		0	0	
58 - Nephrogenic systemic fibrosis	0	0		0	0		0	0		0	0	
995 - Other:	2	3	50.0	2	7	250.0	5	3	−40.0	0	1	
Total	**2**	**4**		**13**	**25**	**92.3**	**10**	**8**	**−20.0**	**0**	**6**	

Table 12
Dermatological pathologies: number of procedures, number of patients treated and number of patients at first diagnosis.

DERMATOLOGY	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
59 - Atopic dermatitis	5	1	−80.0	1	1	0.0	0	0	
60 - Cutaneous T-cell lymphoma/Sezary syndrome	340	781	129.7	27	54	100.0	6	14	133.3
61 - Pemphigus vulgaris	123	118	−4.1	8	15	87.5	1	3	200.0
62 - Pruritus due to biliary cirrhosis	12	4	−66.7	2	2	0.0	2	2	0.0
63 - Psoriasis	0	2		0	1		0	1	
64 - Toxic epidermal necrolysis (TEN) - drugs	13	4	−69.2	3	1	−66.7	3	1	−66.7
65 - Burn shock	0	0		0	0		0	0	
996 - Other:	47	76	61.7	5	6	20.0	5	5	0.0
Total	**540**	**986**	**82.6**	**46**	**80**	**73.9**	**17**	**26**	**52.9**

Table 13
Gastrointestinal disorders: number of procedures, number of patients treated and number of patients at first diagnosis.

GASTROINTESTINAL SYSTEM	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
68 - Acute liver failure-Fulminant hepatitis	26	62	138.5	8	13	62.5	8	10	25.0
69 - Porphyria	0	0		0	0		0	0	
70 - Chronic inflammatory bowel disease	303	124	−59.1	41	16	−61.0	11	6	−45.5
71 - Fulminant Wilson's disease	0	0		0	0		0	0	
998 - Other:	37	63	70.3	11	18	63.6	4	13	225.0
Total	**366**	**249**	**−32.0**	**60**	**47**	**−21.7**	**23**	**29**	**26.1**

Table 14
Metabolic pathologies: number of procedures, number of patients treated and number of patients at first diagnosis.

METABOLISM	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
72 - Familial hypercholesterolaemia	340	264	−22.4	17	11	−35.3	2	1	−50.0
73 - Pancreatitis with hypertriglyceridaemia	73	78	6.8	17	27	58.8	11	19	72.7
74 - Hyper-Lp (a)	70	52	−25.7	3	4	33.3	0	2	
75 - Peripheral vascular disease	48	36	−25.0	4	3	−25.0	4	3	−25.0
76 - Refsum's disease	0	0		0	0		0	0	
999 - Other:	40	45	12.5	28	4	−85.7	1	1	0.0
Total	**571**	**475**	**−16.8**	**69**	**49**	**−29.0**	**18**	**26**	**44.4**

accounted for 25 % in 2019 and 22 % in 2020 (Table 14).

Significant activity in the field of solid organ transplantation was reported: the procedures for ABO compatible kidney transplant - Ac mediated rejection accounted for 35 % in 2019 and 29 % in 2020, however the data are insufficient to be evaluated (Table 15).

The use of therapeutic apheresis in solid organ transplantation has increased over the years, and it is likely that the number of aphaeretic interventions will rise further in this area at all stages, from

Table 15
Solid organ transplant: number of procedures, number of patients treated and number of patients at first diagnosis.

SOLID ORGAN TRANSPLANT	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
77 - Heart Transplant-Recurrent Rejection	121	124	2.5	9	12	33.3	0	3	
78 - Heart transplant - Prophylaxis of rejection	185	421	127.6	8	16	100.0	0	1	
79 - Heart Transplant-Desensitization	0	7		0	2		0	2	
80 - Heart Transplant-Ab-mediated Rejection	45	40	−11.1	9	8	−11.1	7	6	−14.3
81 - Liver Transplant, ABO Desensitization (Living Donor)	0	1		0	1		0	1	
82 - Liver transplant, ABO Desensitization (deceased donor)	76	0	−100.0	1	0	−100.0	0	0	
83 - Liver transplant, Ab Rejection (ABO / HLA)	75	21	−72.0	5	6	20.0	1	4	300.0
84 - Lung Transplant-BOS	16	136	750.0	3	13	333.3	2	7	250.0
85 - Lung Transplant-Ab-Mediated Rejection	26	39	50.0	4	5	25.0	2	5	150.0
86 - Lung Transplant-Desensitisation	0	0		0	0		0	0	
87 - ABO compatible kidney transplant - Ab mediated rejection	405	467	15.3	76	71	−6.6	39	38	−2.6
88 - ABO compatible kidney transplant - Desensitization, living donor	17	31	82.4	3	6	100.0	3	5	66.7
89 - ABO compatible kidney transplant - Desensitization, deceased donor	45	182	304.4	6	19	216.7	5	3	−40.0
90 - ABO Incompatible kidney transplant - Desensitization, living donor	116	134	15.5	17	18	5.9	12	14	16.7
91 - ABO Incompatible Kidney Transplant-Ab mediated Rejection	35	2	−94.3	5	1	−80.0	5	0	−100.0
990 - Other:	0	6		0	1		0	1	
Total	**1162**	**1611**	**38.6**	**146**	**179**	**22.6**	**76**	**90**	**18.4**

Table 16
Other pathologies: number of procedures, number of patients treated and number of patients at first diagnosis.

OTHER	N. Procedures			N. Patients			N. of Patients at first diagnosis		
	2019	2020	Δ%	2019	2020	Δ%	2019	2020	Δ%
92 - Age-related macular degeneration	13	0	−100.0	2	0	−100.0	2	0	−100.0
93 - Dilated cardiomyopathy	0	0		0	0		0	0	
94 - Sudden hearing loss	0	18		0	15		0	3	
95 - HELLP syndrome	5	20	300.0	1	4	300.0	0	2	
96 - Overdose, envenomation, and poisoning	0	7		0	3		0	3	
97 - Sepsis with multiorgan failure	12	24	100.0	2	6	200.0	0	4	
989 - Other:	0	0		0	0		0	0	
Total	**30**	**69**	**130.0**	**5**	**28**	**460.0**	**2**	**12**	**500.0**

desensitisation to rejection.

In the field of pathologies indicated “other” (Table 16) we analysed sepsis with multiorgan failure, which were the most common. However, the number is too small for an outcome assessment.

4. Discussion

The Italian Registry of Therapeutic Apheresis has long been one of the most active registries with significant case studies, comparable with the best-organized Registries in literature, such as the Canadian and French Registries [8–10]. The French Registry, faced with the same difficulties encountered by SIdEM, also decided to converge its data within a public health management system, thus collecting very significant activity data [10].

In Germany, the greatest use of therapeutic apheresis is for familial hypercholesterolemia, the data of which are collected within a dedicated registry [11]. This first survey of therapeutic apheresis procedures was born of the collaboration between SIdEM and the NBC, which funded and developed a dedicated software following the indications of SIdEM. In addition, NBC staff were involved in the data collection and analyses. The participation of apheresis centres was widespread, and in some regions, adhesion was 100 %. The number of therapeutic apheresis procedures reported (28550) rose by 21 % compared to 2019, and the number of patients treated (6321) also increased by 20 %. The number of paediatric patients reported increased by 38 %, (6321 vs 5253) while there was a 17 % increase in the number of emergency procedures performed. The increasing number was mainly due to the progressive adhesion of the Centres to the Registry, rather than an actual increase in activity. In fact, in 2020, the numbers were in line with the data collected and documented in the previous and most recent registries [2]. As for side effects and adverse events, therapeutic apheresis has proved to be a treatment with high safety margins. Adverse events to therapeutic apheresis procedures reported concerned 5% of the total performed in 2019 and 4% in 2020.These were mainly mild reactions that decreased by 5% in 2020 compared to 2019. However, to date, only a few centres have entered all their data, and we hope that in time their entries will be increasingly complete to allow a reliable analysis of all parameters. On the other hand, albeit with limited numbers, the average/moderate reactions increased and were related to autologous hematopoietic stem cell (HSC) collection (51 % of the total in 2020) and plasma exchange procedures (42 % of the total in 2020). These data, as well as the overall number of adverse events, remain in line with the literature [2,3,12–14].

The index between the procedures performed and the number of patients treated was 1.4 for the collection of HSCs and 15.6 for cytapheresis in both years, and 4.1 in 2020 and 3.5 in 2019 for cytapheresis. The outcomes of the diseases treated indicate that disease remission is possible in some cases and that it is important to continue to monitor this activity to study other potential uses for therapeutic apheresis. However, it is necessary to increase the number of data entries, especially for outcomes and adverse events.

In conclusion, the first experience of the Italian Therapeutic Apheresis Registry in SISTRA appears positive, although as we are speaking of a completely new system, we deem it necessary to continue to provide assistance for operators as regards their registration. The result obtained, however, confirms the interest in keeping the Registry active as a monitoring tool for both activities and areas of application: also from this point of view, apheresis is constantly evolving. Although the number of both haematological and solid organ transplants is constantly on the increase, the procedure is still more frequently used for neurological diseases. It is desirable that the insertion of data, especially outcomes and adverse events, can be numerically more substantial, so as to allow a more complete assessment of therapeutic apheresis procedures.

CRediT authorship contribution statement

Liviana Catalano, Giustina de Silvestro, Giuseppe Marano: Conceptualization, Methodology, Software validation, Writing. **Vanessa Piccinini:** Data curation. **Simonetta Pupella, Angelo Ostuni, Vincenzo de Angelis:** Supervision.

Declaration of Competing Interest

The authors declare that they have no conflict of interest relevant to the manuscript submitted to Transfusion and Apheresis Science

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