透視兒童洗腎

洗腎兒童的溫馨故事 – 林口長庚篇

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大綱

- 兒童末期腎臟病(ESKD) 發生率和盛行率
- 兒童末期腎臟病(ESKD)原因
- 兒童末期腎臟病(ESKD)治療模式
- 末期腎臟病(ESKD)對孩童的影響(臨床共病)
- 病例分享

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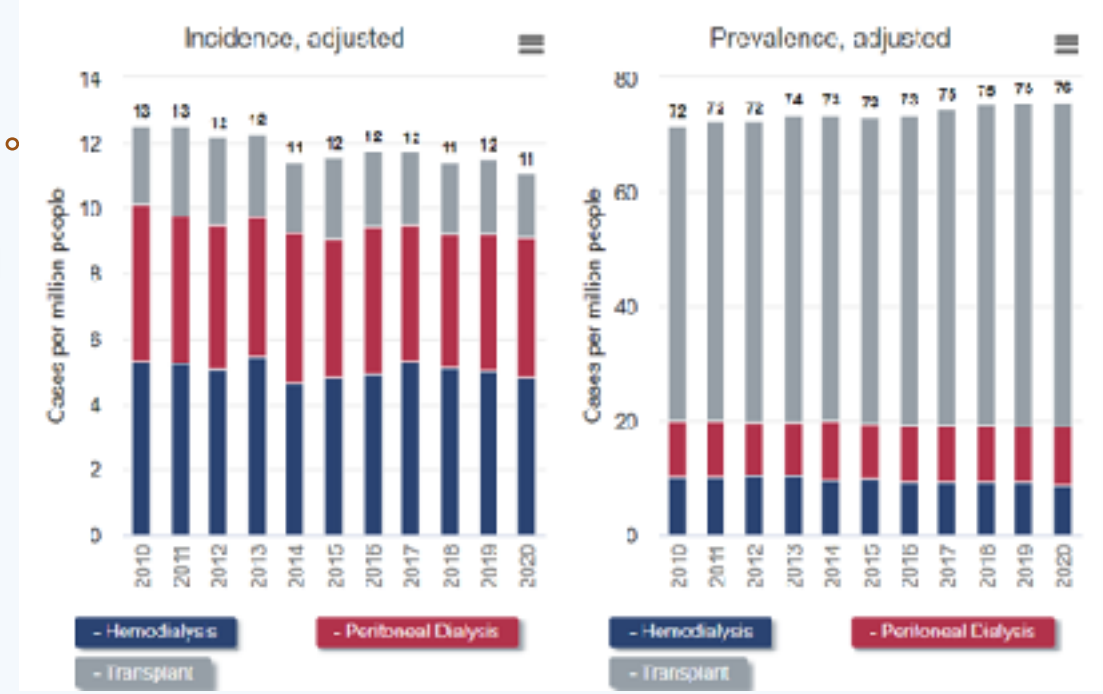
兒童末期腎臟病(ESKD) 的發生率和盛行率 (2010-2020)

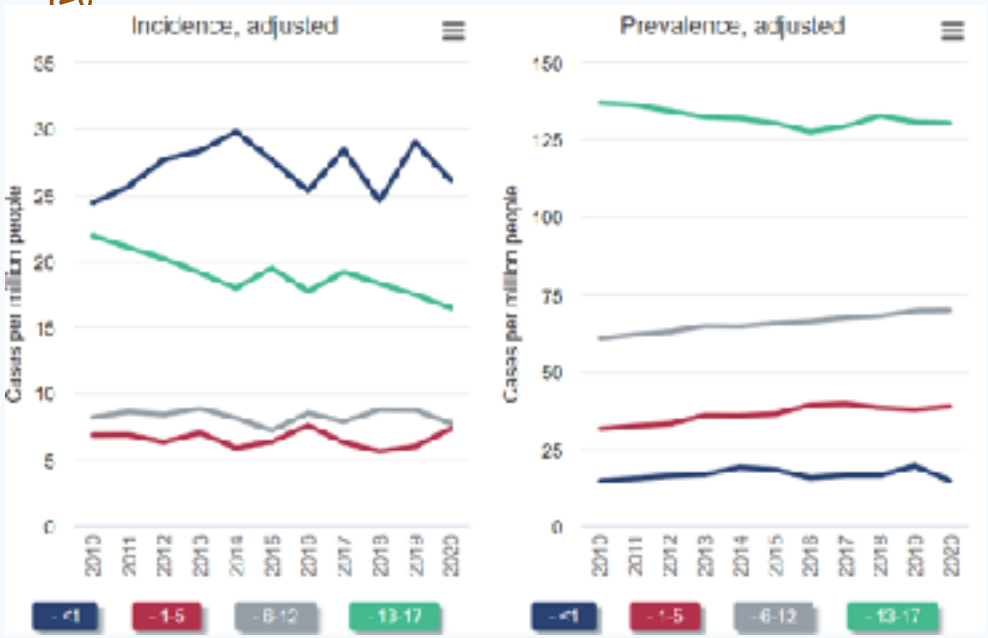
根據2022 美國USRDS年報顯示0-17歲兒童末期腎臟病(ESRD) 的發生率和盛行率:

- **兒童ESKD的發生率** 從2010 年的每百萬人口13 例 (13 pmp)**下降** 到2020 年的每百萬人口11 例 (11 pmp)。
- 與成人不同，兒童 ESRD 的發生率或盛行率**沒有明顯變化**。
- **接受血液透析(HD)和腎臟移植(KT) 的情況相對穩定**，而腹膜透析 (PD) 的發生率則下降。
- 兒童 ESRD 盛行率從 72 pmp 增加到 76 pmp，這主要是由於**接受腎臟移植的兒童盛行率增加**所致。

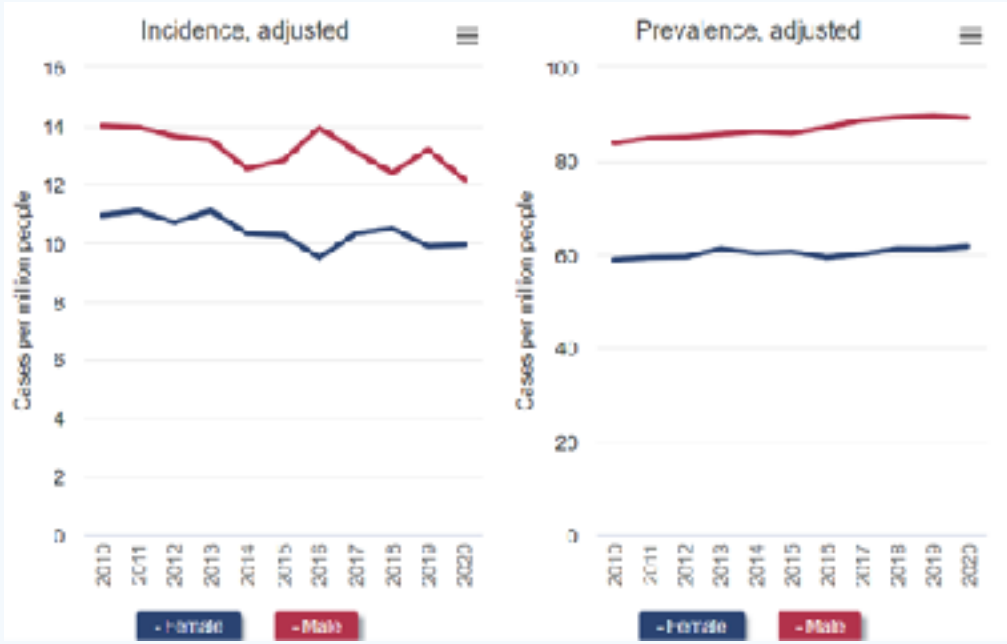


2022 美國USRDS: 兒童 ESKD 發生率和盛行率（按**年齡**和**性別**）

- ESRD 事件發生率在**<u>1歲以下</u>和<u>13-17歲兒童中最高</u>**，而 1-12 歲兒童則較低。

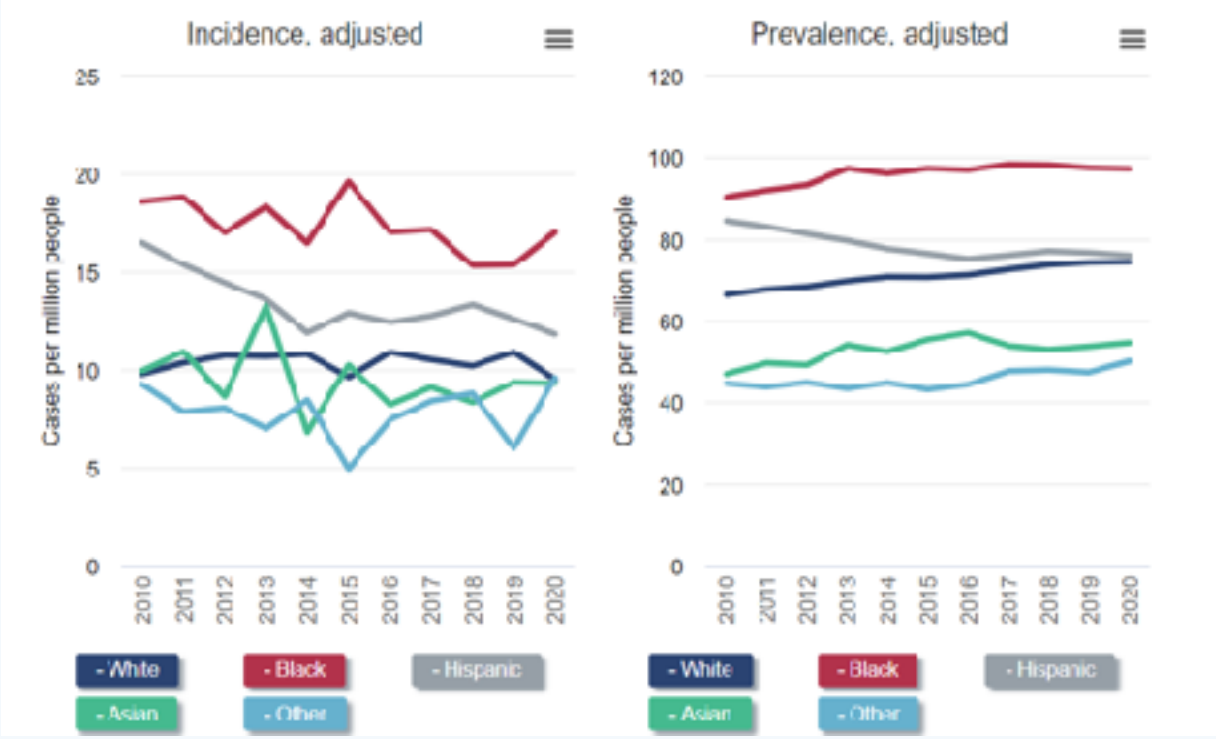


- 調整後的 ESRD 盛行率**<u>男孩</u>**比女孩**高近 50%**。



2022 美國USRDS: 兒童 ESKD 發生率和盛行率 （按種族）

- 與其他族群相比，**黑人兒童的ESRD率最高**，顯著高於其他族群。
- 亞洲兒童和其他種族/族裔群體的兒童 ESRD 盛行率最低。



	2010	2011	2012	2013	2014
總計	29	29	35	29	25
性別					
男性	13 (44.8%)	14 (48.3%)	23 (65.7%)	16 (55.2%)	18 (72.0%)
女性	16 (55.2%)	15 (51.7%)	12 (34.3%)	13 (44.8%)	7 (28.0%)
年齡別					
<6	0 (0.0%)	1 (3.4%)	2 (5.7%)	3 (10.3%)	1 (4.0%)
6-11	3 (10.3%)	3 (10.3%)	3 (8.6%)	5 (17.2%)	4 (16.0%)
12-19	26 (89.7%)	25 (86.2%)	30 (85.7%)	21 (72.4%)	20 (80.0%)
透析模式					
血液透析	16 (55.2%)	14 (48.3%)	17 (48.6%)	14 (48.3%)	9 (36.0%)
腹膜透析	13 (44.8%)	15 (51.7%)	18 (45.4%)	15 (51.7%)	16 (64.0%)

台灣兒童末期腎臟病概況

- 每年25-35新發透析病患 (new cases)
- 性別:小兒男性透析發生數較女性多
- 年齡: 12-19 歲發生數最多
- 透析模式: 腹膜透析 較多

資料來源: 2016年台灣腎病年報

大綱

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全球各國針對小於19歲罹患慢性腎臟病或末期腎病變孩童病因之回溯性研究

Table 1 Selected studies on the causes of chronic kidney disease in children

	Causes of CKD (兒童慢性腎臟病原因)			Causes of ESRD (兒童末期腎臟病原因)			
Study [reference]	NAPRTCS [12] 北美	Italian Registry [5] 義大利	Belgian Registry [13] 比利時	ANZDATA [27] 澳洲紐西蘭	ESPN/ERA-EDTA Registry 歐洲	UK Renal Registry 英國	Japanese [30] 日本
Population	CKD (GFR<75)	CKD (GFR<75)	CKD (GFR<60)	ESRD (RRT)	ESRD (RRT)	ESRD (RRT)	ESRD (RRT)
Age range	0–20	0–19	0–19	0–19	0–15	0–15	0–19
Patients	Registered 1994–2007	Incident 1990–2000	Incident 2001–2005	Incident 2003–2008	Incident 2008	Incident 2004–2008	Prevalent 199
Number of cases	7,037	1,197	143	369	499	428	582
Etiology							
CAKUT	3,361 (48%)	689 (58%)	84 (59%)	127 (34%)	182 (36%)	184 (43%)	208 (36%)
Hypodysplasia±reflux nephropathy	1,907	516	66	95		135	198
Obstructive uropathy	1,454	173	18	32		49	10
Glomerulonephritis	993 (14%)	55 (5%)	10 (7%)	108 (29%)	76 (15%)	78 (18%)	130 (22%)
HUS	141 (2%)	43 (4%)	9 (6%)	9 (2%)	29 (6%)		13 (2%)
Hereditary nephropathy	717 (10%)	186 (15%)	27 (19%)		112 (22%)		69 (12%)
Congenital NS	75	13	5	7		15	34
Metabolic disease			5		17	18	
Cystinosis	104	22	2	4			2
Cystic kidney disease	368 (5%)	101 (8%)	13 (9%)	25 (7%)	59 (12%)	49 (11%)	35 (6%)
Ischemic renal failure	158 (2%)	49 (4%)	3 (2%)	8 (2%)	11 (2%)		11 (2%)
Miscellaneous	1,485 (21%)	122 (10%)	10 (7%)	65 (18%)	52 (10%)	19 (4%)	83 (14%)
Missing/unknown	182 (3%)	40 (3%)		16 (4%)	37 (7%)	65 (15%)	34 (6%)

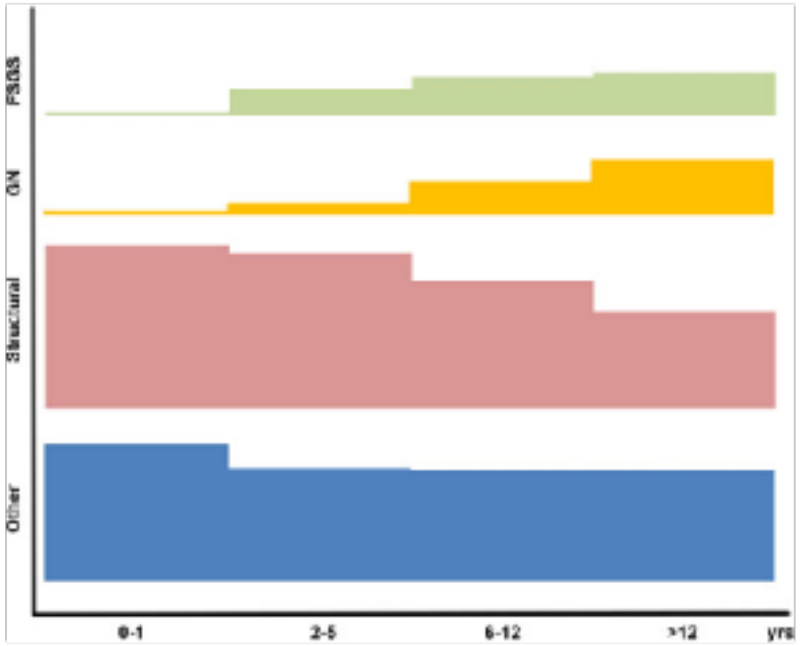
結果顯示: 先天腎臟泌尿道結構異常特別是腎臟先天發育不良、逆流性腎病變和阻塞性腎病變是造成孩童慢性腎病變及末期腎病變最常見原因。

Etiologies of paediatric CKD/ESRD : GN vs. CAKUT

Table 1. Frequency of different diagnostic groups as causes of CKD and ESRD in children

	Frequency as cause of CKD [12, 13, 26]	Aetiology	Proportion of cases of CKD determined by specific diagnostic sub-groups [26]	Frequency as cause of ESRD [12–15, 19]
Glomerular diseases	6.8–20.5%	SRNS	10.4%	15.2–24.3%
		Glomerulonephritis	8.1%	
		Thrombotic microangiopathies (aHUS)	2.0%	
Structural and other	56–57.6%	CAKUT	49.1%	38.3–39.5%
		Ciliopathies	5.3%	
		Nephrolithiasis, nephrocalcinosis	1.6%	

Impact of different causes of CKD in children among age groups



- Glomerular diseases (腎絲球疾病) significantly increase in older children, while structural disorders (泌尿道結構異常) are more common as causes of CKD in infants and younger children.
- Gender difference (性別差異)
  CKD: male (男生)> female (女生), due to high frequency of CAKUT (先天腎臟泌尿道結構異常) in males
- Race difference (種族差異)
  (1) In North America, African-American children > Caucasian Children
  (2) In Australia and New Zealand, Aborgines and Maoris children > the reminder of pediatric population

Clinical Kidney Journal, 2016, vol. 9, no. 4, 583–591

Table 1 Primary causes of chronic kidney disease (CKD) in children

	N (%)
Glomerular	370 (48.9 %)
Primary glomerulonephritis	150 (19.8 %)
Secondary glomerulonephritis	
Lupus nephritis	122 (16.1 %)
Henoch Schönlein nephritis	6 (0.8 %)
Others	4 (0.5 %)
Chronic glomerulonephritis	71 (9.4 %)
Congenital nephritis	13 (1.7 %)
DM nephropathy	4 (0.5 %)
Non-glomerular	387 (51.1 %)
Renal agenesis	
Congenital	61 (8.1 %)
Acquired	17 (2.2 %)
Renal atrophy/dysplasia	39 (5.2 %)
Reflux nephropathy	94 (12.4 %)
Obstructive uropathy	60 (7.9 %)
Cystic kidney disease	76 (10.0 %)
Renal tubulopathy	15 (2.0 %)
Renal infarct	9 (1.2 %)
Others	16 (2.1 %)
Total	757 (100 %)

Pediatr Nephrol (2016) 31:1113–1120

台灣孩童慢性腎臟病發生常見原因:

(1) 腎絲球疾病(glomerular disease)占48.9 %: 主要是原發性腎炎(19.8%)或自體免疫性疾病續發之腎炎如紅斑性狼瘡腎炎(16.1%)引起。

(2) 非腎絲球疾病 (non-glomerular disease)占51.1 %: 主要是先天腎臟泌尿道結構異常(**CAKUT**, congenital anomalies of kidney and urinary tract)引起包括腎臟未發育(8.1%)或發育不良(5.2%)、逆流性腎病變(12.4%)或是阻塞性腎病變(7.9%)引起。

(3) 囊性腎病變 (10%)

台灣孩童慢性腎臟病發生原因和年齡、性別的關係:

(1) 七歲以前:
主要以非腎絲球疾病(先天腎臟泌尿道結構異常)引起

(2)七歲以後:主要是腎絲球疾病引起

(3)男生(孩)發生慢性腎臟病的情況比女生孩高

Variable	All (N = 744)	Etiology of CKD		p value
		Glomerular (n = 358)	Nonglomerular (n = 386)	
Age at registry (n = 757)				<0.001*
1–5 years	144 (19.0 %)	25 (6.8 %)	119 (30.7 %)	
6–11 years	272 (35.9 %)	122 (33.0 %)	150 (38.8 %)	
12–17 years	341 (45.0 %)	223 (60.3 %)	118 30.5 %)	
Gender, males (n = 757)	397 (52.4 %)	175 (47.3 %)	222 (57.4 %)	0.003*

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台灣孩童慢性腎臟病發生原因和年齡、性別的關係:

(1) 七歲以前:
主要以非腎絲球疾病(先天腎臟泌尿道結構異常)引起。

(2)七歲以後:主要是腎絲球疾病引起。

(3)男生發生慢性腎臟病的情況比女生高。

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Original Article

The pathological spectrum of pediatric kidney disease: 18-Year experience from a single tertiary care center in northern Taiwan

Chen-Wei Yen [a], Tai-Di Chen [b,c], Tzung-Hai Yen [c,d], Mei-Ching Yu [a,c,*]

在林口長庚醫院進行的18年回顧性研究中，結果顯示
(1) **LN**(紅斑性狼瘡腎炎)、**MCD**相關的**INS**(兒童原發性腎病症候群)和原發性**IgAN** 仍然是腎臟切片證實兒童和青少年疾病的主要疾病。
(2) 此外，我們發現2002年至2017年的研究期間，兒童腎臟病的(病理組織)模式並沒有顯著變化.

Table 3 The comparison of age disparity between the two groups, aged <12 years and 12–18 years, in the histopathological profiles among the two consecutive periods, from 2002 to 2010 and from 2011 to 2020.

Renal pathology (n)	<12 years old, n (%)			12 – 18 years old, n (%)		
	2002 to 2010	2011 to 2020	*P* value	2002 to 2010	2011 to 2020	*P* value
LN (139)	12 (21.4)	12 (15.4)	0.372	27 (55.1)	88 (56.4)	0.873
MCD (61)	16 (28.6)	18 (23.1)	0.474	11 (22.4)	16 (10.3)	0.181
IgAN (34)	7 (12.5)	7 (9.0)	0.514	6 (12.2)	14 (9.0)	0.503
FSGS (27)	4 (7.1)	10 (12.8)	0.293	3 (6.1)	10 (6.4)	0.943
HSPN (7)	2 (3.6)	1 (1.3)	0.381	0 (0)	4 (2.6)	0.260
APSGN (5)	5 (8.9)	0 (0)	0.007*	0 (0)	0 (0)	–
ANCA-associated GN (4)	2 (3.6)	2 (2.6)	0.738	0 (0)	0 (0)	–
TMA (4)	0 (0)	2 (2.6)	0.230	0 (0)	2 (1.3)	0.428
TID (28)	2 (3.6)	13 (16.7)	0.082	1 (2.0)	12 (7.7)	0.158
Hereditary diseases (8)[a]	3 (5.4)	2 (2.6)	0.404	0 (0)	3 (1.9)	0.331
Other diseases (5)[b]	0 (0)	2 (2.6)	0.230	1 (2.0)	2 (1.3)	0.701
Insufficiency for diagnosis (17)	3 (5.4)	9 (11.5)	0.219	0 (0)	5 (3.2)	0.206
Total (339)	**56 (100)**	**78 (100)**		**49 (100)**	**156 (100)**	

*P value < 0.05.

[a] Hereditary disease includes thin basement membrane disease, Alport syndrome, autosomal recessive polycystic kidney disease and papillorenal syndrome (renal coloboma syndrome).

[b] Others include C3 Glomerulopathy, cyanotic nephropathy, diabetic nephropathy, and IgM nephropathy.

Pediatr Neonatol. 2023 Jan;64(1):26-31

大綱

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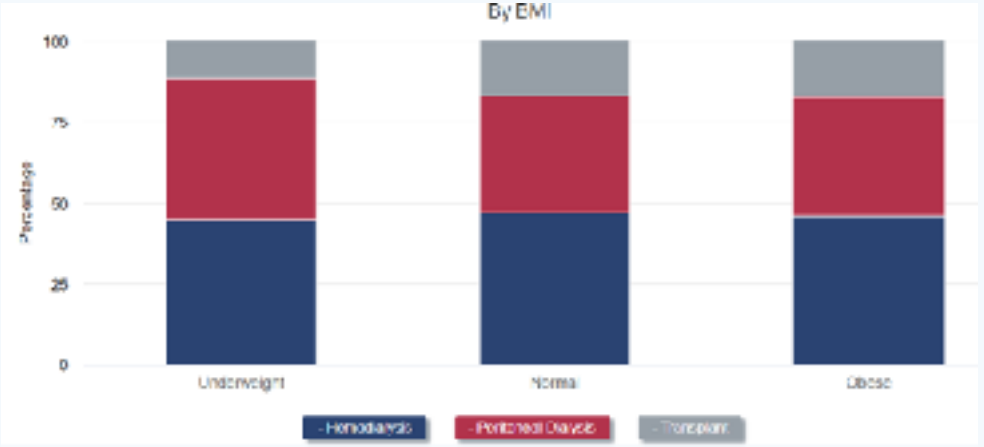
2022 美國USRDS: 兒童發生ESKD時的治療方式以年齡(age)和身體質量指數(BMI)分布

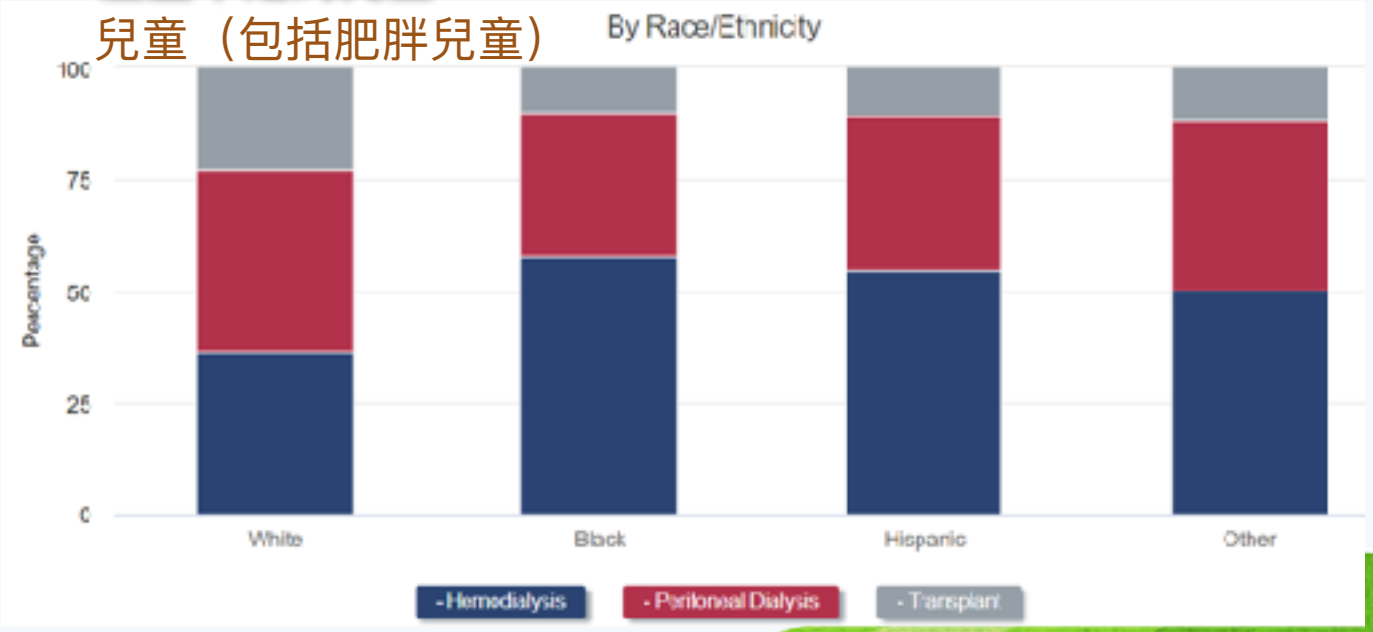
- 依病患年齡劃分ESRD 兒童治療方式 (2016 年至 2020 年):
- 在**1歲以下**的兒童中，91.5%選擇PD。
- 隨著年齡的增長，以HD為治療方式的百分比增加。**13-17 歲兒童中，以HD為初始治療方式**的人數是

- **BMI過輕**的兒童**接受腎臟移植的頻率低**於BMI較高的兒童(包括肥胖兒童)。



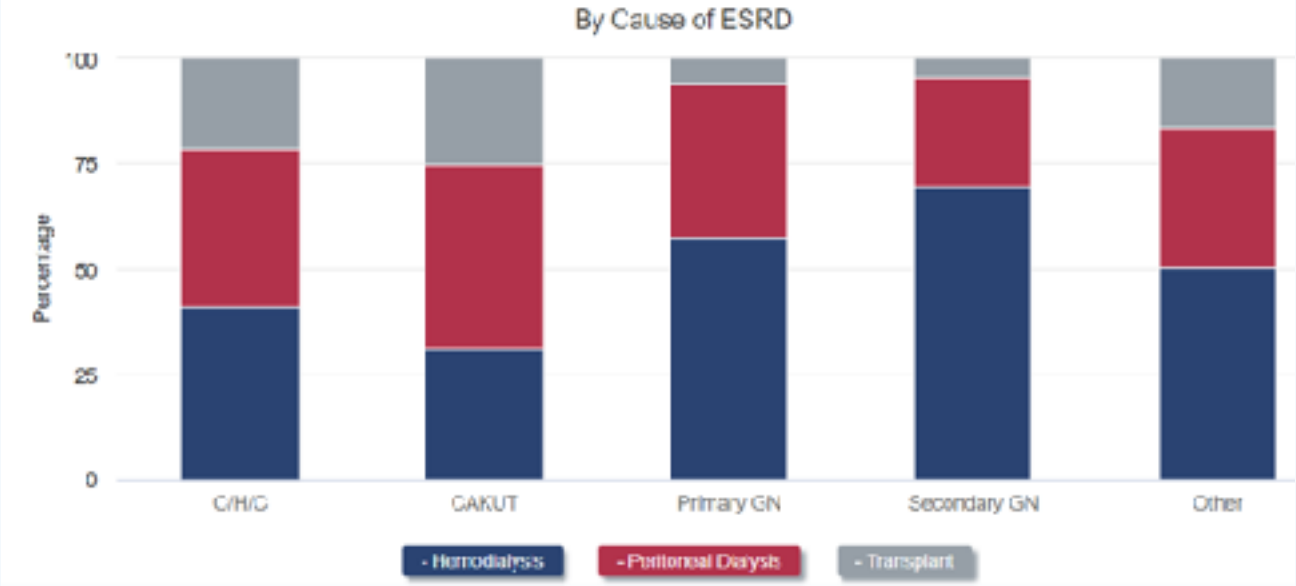
2022 美國USRDS: 兒童發生ESKD時的治療方式以種族(Race/Ethnicity)分布

- 與PD 相比，更多**黑人**（57.8% vs 32.3%）和**西班牙裔兒童**（54.7% vs 34.5%）開始接受HD 替代治療）。
- 而**白人兒童則開始選擇PD**多於HD （40.6 % vs 36.5%）。
- **白人兒童接受腎臟移植 (KT)**是黑人兒童的兩倍以上（22.9% 對 9.9%）。
- 對於所有**非白人兒童，HD**是先發性腎移植(pre-emptive KT) 作為初始治療方式的 4 倍以上（而對於白人兒童而言，
- 患有**先天性腎臟病**的兒童在發生ESKD時接受KT的頻率比患有原發性或繼發性GN的兒童要高得多。
- **體重不足的兒童**接受KT的頻率低於體重指數較高的兒童（包括肥胖兒童）



2022 美國USRDS: 兒童發生ESKD時的治療方式以原始腎臟疾病分布

- 接受HD比例在**患有 GN 的 ESKD兒童高**於非 GN 的兒童。(這些差異可能部分是由 ESRD 發病年齡的差異所造成的)



- C/H/C: cystic/hereditary/congenital diseases
- CAKUT: congenital anomalies of the kidney and urinary tract
- GN: glomerulonephritis

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- 性別:小兒男性透析發生數較女性多
- 年齡: 12-19 歲發生數最多
- 透析模式: 腹膜透析 較多

資料來源: 2016年台灣腎病年報

大綱

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末期腎臟病孩童不同於成人病患:

隨著透析治療的時間或等待非親屬腎臟捐贈的時間增加

(1)容易發生腎臟以外的嚴重或不可逆的併發症 *

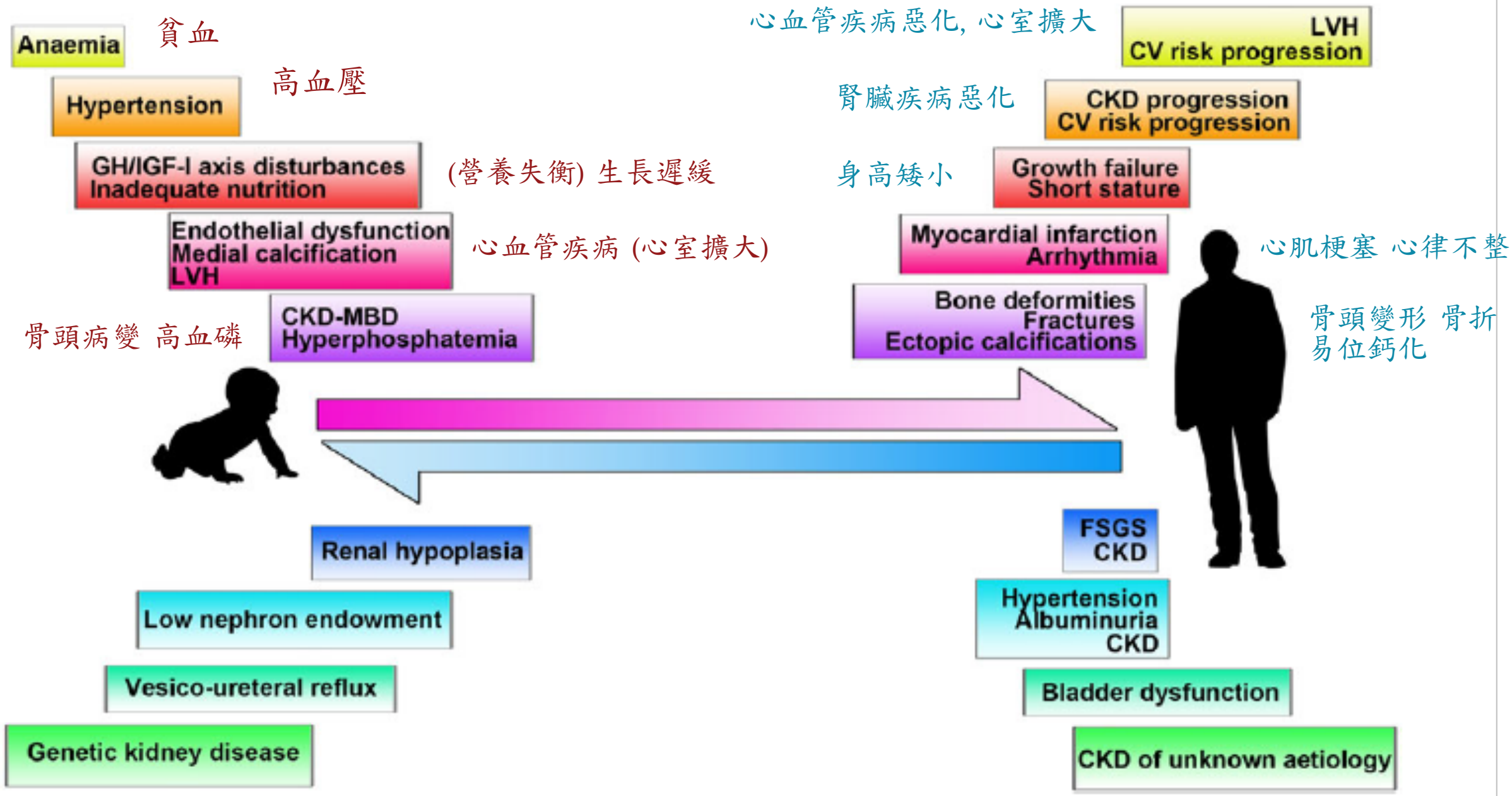
- 腦部病變
- “頑固”高血壓→ 心血管疾病
- 腎性骨質病變
- 貧血問題

(2)身長發育嚴重落後

(3)疫苗預防接種問題

(4)教育問題

(5)情緒問題



Clinical Kidney Journal, 2016, vol. 9, no. 4, 583–591

兒童案例 1

親屬活體移植治療尿毒症

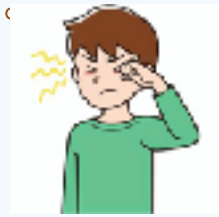
18歲男孩羅X鋒 ，因罹患雙側先天腎臟發育不良 (congenital renal hypoplasia)，腎功能持續惡化而導致末期腎臟病(尿毒症)。在與父母親詳細討論後，決定不考慮透析治療，於是在14歲時接受前置性腎臟移植治療(preemptive kidney transplantation, on February 21th 2020)。

成功移植之後，腎功能很快回復正常。然而，在移植半年後，男孩因為服藥順從性不佳，進而發生移植腎排斥情形，經過將近一年多的免疫抑制藥物、諸多生物製劑、免疫球蛋白和多次血漿置換術等治療後，移植腎功能依然沒能獲得明顯改善，最終需要接受每周三次血液透析治療 。

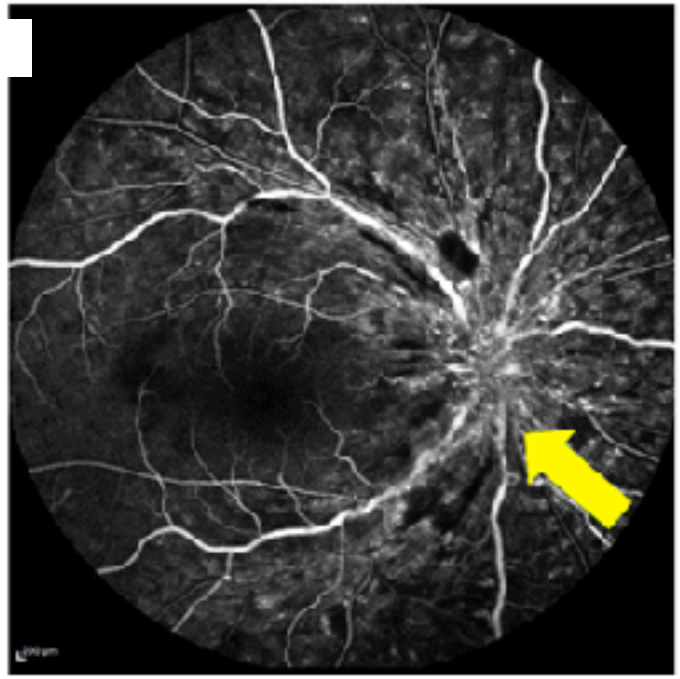
突發嚴重雙眼視覺缺損和障礙

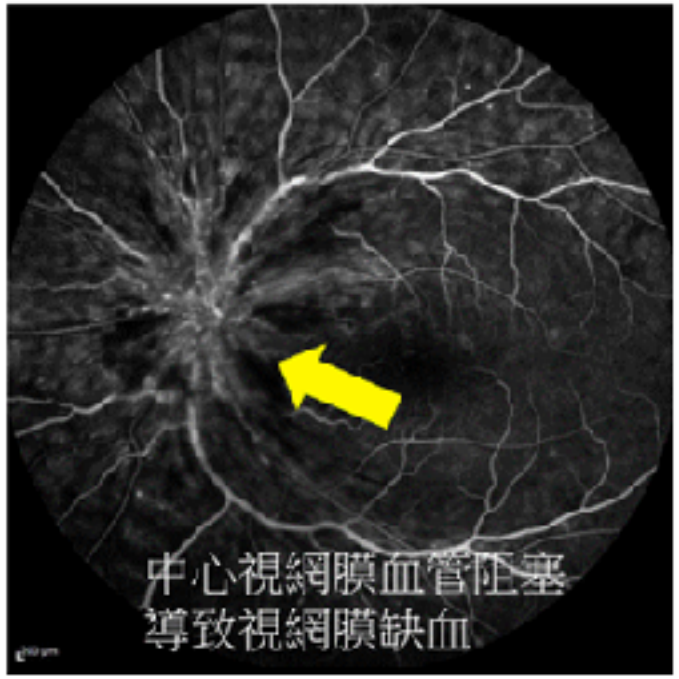
然而，在開始接受血液透析治療兩周後，男孩突然出現雙眼漸進性視野模糊障礙情形 (on August 17th 2021)。男孩意識清楚，腦部電腦斷層檢查也沒有腦部出血等其他異常。雖有高血壓情形，在經過藥物治療後，可以獲得良好控制。同時也沒有頭痛和其他不適情形。

在接受眼科醫師進一步檢查後發現左眼對光完全無反應，右眼也有嚴重視覺缺損和障礙現象。眼部光學斷層掃描(optical coherence tomography)和視網膜電圖檢查結果，懷疑可能和視網膜動(靜)脈閉塞引起前部視神經缺血性病變有關 (如圖示)。



視網膜血管阻塞導致缺血

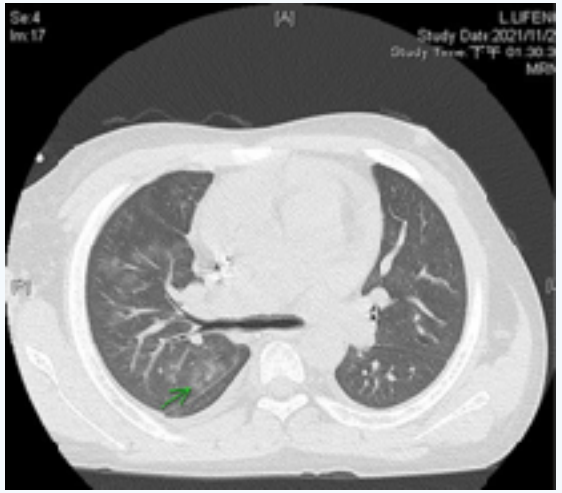




補體因子CHF相關非典型溶血性尿毒症候群

而回溯發生眼睛病變前一個月前，男孩曾因呼吸窘迫，身上出現多處瘀斑，不明原因嚴重貧血和血小板低下症於兒童加護病房接受治療。即便周邊血液抹片並沒有微小血管性溶血性貧血(microangiopathic hemolytic anemia: fragmented red blood cells/schizocytosis)的明顯證據，但諸多跡象讓醫療團隊不禁懷疑是否有非典型溶血性尿毒症候群(atypical hemolytic uremic syndrome, aHUS)的可能性。

而後續的基因檢測也證實為補體因子 **complement factor H (CFH)**有關的病變 。在罕病通過，申請藥物和等待治療的過程中，男孩也曾經發生咳血，所幸肺出血狀況沒有持續惡化，危及生命。



最終在五個月後獲得藥物(Eculizumab)許可開始進行治療(January 13th 2022)，然而眼睛病變卻也無法逆轉，左眼失明同時右眼嚴重視野缺陷。

Table 4. Reports of organ system complications in aHUS.

Organ System Complications Due to aHUS					
Organ System	**Authors**	**Year**	**Sample Size**	**Age**	**Outcome**
Neurological	Gulleroglu et al.	2013	2	14	Neurologic symptoms and irregular cerebral MRI results
	Diamante et al.	2014	1	<18	Multifocal hyperintensities and altered consciousness
Cardiovascular	Hu et al.	2015	1	0.75	Cardiomyopathy and altered cardiac function
	Vilalta et al.	2012	1	1	
	Neuhaus et al.	1997		23	
	Davin et al.	2010	1	15	Middle and anterior cerebral artery stenosis
Pulmonary	Johnsun et al.	2014	71	-	21% of aHUS patients developed respiratory failure
Ocular	Zhang et al.	2014	1	11	Decreased visual acuity (20/100 in the right eye, 20/200 in the left eye) Intraretinal hemorrhages, Venous stasis retinopathy, and Vein occlusions
Gastrointestinal	Besbas et al.	2017	146	-	10% displayed vomiting, cholelithiasis, transaminitis, pancreatitis, hepatitis, and GI bleeding
	Dragon-Durey et al.	2010	45	-	<80% of patients with anti-CFH antibodies had GI symptoms
	Roman-Ortiz et al.	2014	1	9	Abdominal pain

Reports of organ system complications in atypical hemolytic uremic syndrome patients/cohorts. MRI: magnetic resonance imaging; GI: gastrointestinal; CFH: complement factor H.

Table 3. Clinical manifestations of aHUS based on organ system.

Organ System	Clinical Manifestations		Reported Efficacy of Eculizumab
Renal	Glomerular thrombotic microangiopathy, Arterial TMA, and Cortical necrosis		Yes
Neurological	Seizures, Headache, Altered consciousness, Hemiparesis, Vision loss, Hallucinations, Encephalopathy	Agitation, Confusion, Reduced reflexes, Hemiplegia, Nystagmus, Diplopia, Focal neurologic deficits, Coma	Yes
Pulmonary	Pulmonary embolism, Hemorrhage, Edema, Respiratory failure		N/A
Dermatologic	Peripheral gangrene, Ischemia, Cutaneous rashes		Yes
Cardiovascular	Hypertrophic cardiomyopathy, Left ventricular hypertrophy, Elevated CK-MB level, Dilated cardiomyopathy, Valve insufficiency	Tachycardia, Intracardiac thrombus, Steno-occlusive arterial disease in large arterial vessels (i.e., middle and anterior cerebral artery stenosis)	Yes
Ocular	Reduced visual acuity, Ocular pain, Visual scotomas, Diplopia, Blurred vision	Optic disc edema, Bilateral flame shaped intraretinal hemorrhage, Tortuosity, Venous stasis retinopathy	Yes
Gastrointestinal	Vomiting, Cholelithiasis, Transaminitis, Pancreatitis,	Hepatitis, Gastrointestinal bleeding, Abdominal pain	Yes

Clinical manifestations of aHUS based on organ system and documented effectiveness of Eculizumab.

Skeletal system: rhabdomyolysis

Pediatric Atypical Hemolytic Uremic Syndrome Advances. Raina R, et al. Cells. 2021 Dec 18;10(12):3580

Recurrent ocular involvement in pediatric atypical hemolytic uremic syndrome: A case report

Zheng et al. Pediatr Ophthalmol Strabismus. 2014 Oct 1;51:e62-5.

The case of an 11-year-old girl diagnosed as having atypical HUS who presented with bilateral central retinal vein occlusions with macular subhyaloid hemorrhage during her initial onset and ophthalmoplegia, diplopia, and optic disc edema during her relapsing episode 1 year later is described. All ocular manifestations occurred in the convalescence phase of atypical HUS. No other extrarenal complications were found and full recovery was achieved following typical treatment for atypical HUS (ie, plasma infusion, steroid, and supportive therapy).

描述了一名被診斷為非典型HUS 的11 歲女孩的病例，她在初次發病時出現雙側視網膜中央靜脈阻塞並伴有黃斑玻璃體下出血，1 年後復發時出現眼肌麻痺、複視和視盤水腫。 所有眼部表現均發生在非典型 HUS 的恢復期。 沒有發現其他腎外併發症，並且在非典型 HUS 的典型治療（即血漿輸注、類固醇和支持性治療）後實現了完全康復。

兒童案例 2

腎臟移植是兒童慢性腎臟病最佳的治療方式

病患蘇X維，現年15歲之男童，出生後不久(約15天大)隨即發生不明原因意識障礙和昏迷情況，於林口長庚醫院新生兒加護病房住院治療達一個月之久，經診斷發現有腎功能異常、電解質異常和代謝性酸血症等情況，經腎臟超音波和相關影像檢查診斷可能為雙側腎臟發育不良(Bilateral congenital renal hypoplasia)合併膀胱輸尿管尿逆流(Vesicoureteral reflux)之先天腎臟泌尿系統結構異常。 隨著腎功能持續惡化，病童於5歲時便因為尿毒症開始接受長期腹膜透析治療。

幸運地，在2014年8月23日 (6歲)於林口長庚醫院接受非活體/大愛腎臟移植（Deceased-donor kidney transplantation）。腎功能在成功移植後很快回復正常。

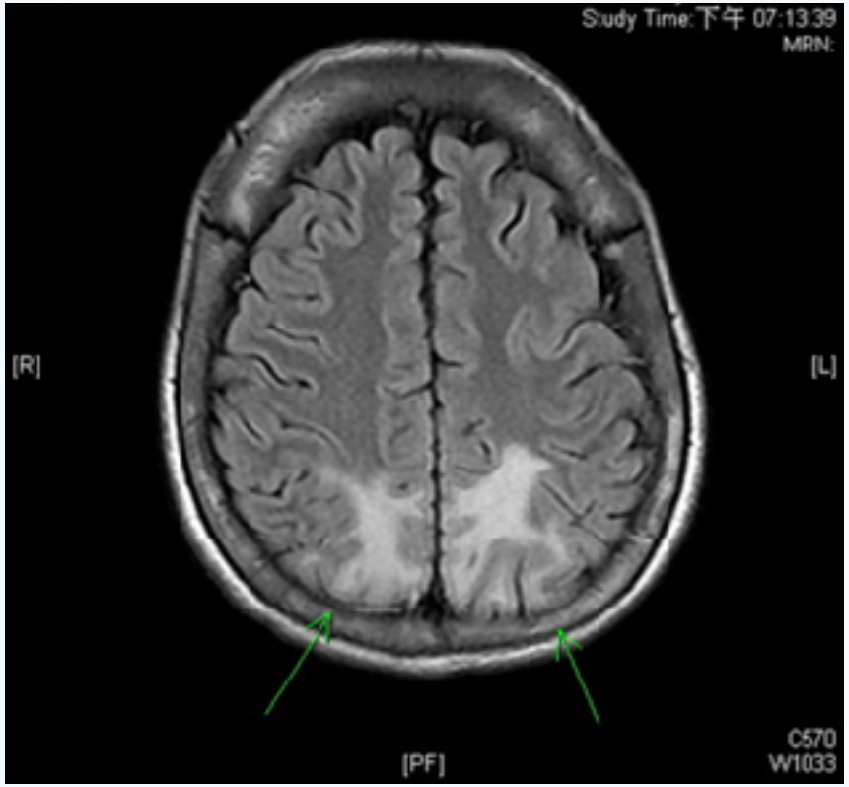
不明原因的癲癇發生

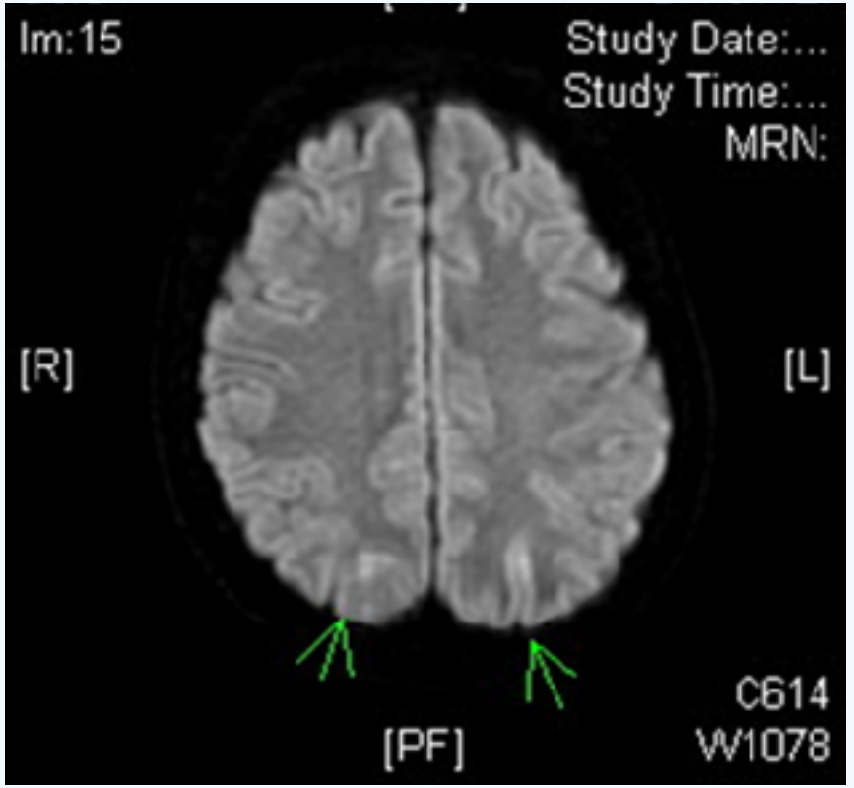
然而自2018年6月(腎臟移植後約4年後)開始出現移植腎功能異常情形，並且移植腎功能呈現持續惡化的情況。在2015年5月9日當日突然發生不明原因且多次全身型僵直-陣攣性癲癇(Generalized tonic-clonic seizure, **GTC**) 合併意識障礙，當時有短暫且輕微體溫略高的情形但並沒有發生明顯惡性高血壓的情形。住院期間腦部電腦斷層檢查無腦部出血情況，且之後的腦部核磁共振檢查明確顯示為可逆性後腦病變症候群 (Posterior reversible encephalopathy syndrome, **PRES**) 。

當時對PRES發生的原因並不是很確定。另一方面，因移植腎功能持續異常，病童共接受三次移植腎切片手術檢查，移植腎病理報告顯示有急性細胞性排斥 (Active T-cell mediated rejection) 並且懷疑有新形成之局灶節段性腎小球硬化症（De novo focal segmental glomerulosclerosis, FSGS）之可能性。然而即便給予高劑量類固醇、生物製劑(Rituximab)和多次血漿置換術(Double filtration plasmapheresis, DFPP)治療後，移植腎功能仍然沒有獲得明顯改善[3] 因此，於2020年12月16日因為移植腎衰竭又再次接受腹膜透析治療。

可逆性後腦病變症候群 (posterior reversible encephalopathy, PRES)

腦部核磁共振影像檢查 (2019/05/13)





不明原因嚴重貧血、血小板低下和間歇性嚴重高血壓

然而，回溯該男童治療移植腎功能異常期間的血液檢驗報告，顯示多次不明原因嚴重貧血、血小板低下症**(<150,000/ul)** 或血小板下降變化超過**25%**的情況。同時，也曾出現不明原因嚴重惡性高血壓 ，需要三種以上的降血壓藥治療 (SBP >170-180 mmHg)。有一段時間又突然血壓改善到只需要一種，或是不需要血壓藥治療的情況。而這種間歇性惡性高血壓現象在進入長期腹膜透析治療後，也是斷斷續續發生。同時在穩定透析和規律藥物治療（包括紅血球生成因子注射），病童也沒有任何感染症和明顯腸胃道出血等不適情況下，血色素會無預期下降到只有5.7 ~ 6.5 mg/dL (嚴重貧血)，並且血小板濃度下降可達35%變化。

在後續相關檢驗(查)排除多種原因引起TMA的疾病。最終基因檢測發現有補體因子(complement factor) 突變 ，最終確診為非典型溶血性尿毒症候群(aHUS)所致。

What is aHUS ?

a typical

- aHUS is not typical because it is not caused by Shiga toxin-producing *Escherichia coli* (STEC)[1]

H aemolytic

- aHUS is characterised by nonimmune, intravascular, mechanical haemolysis (eg, the presence of schistocytes)[2]

U raemic

- aHUS typically causes uraemia, which is when waste products that are normally excreted in urine build up in the blood[3]
- ~20% of patients with aHUS do not present with signs of uraemia[4]

S yndrome

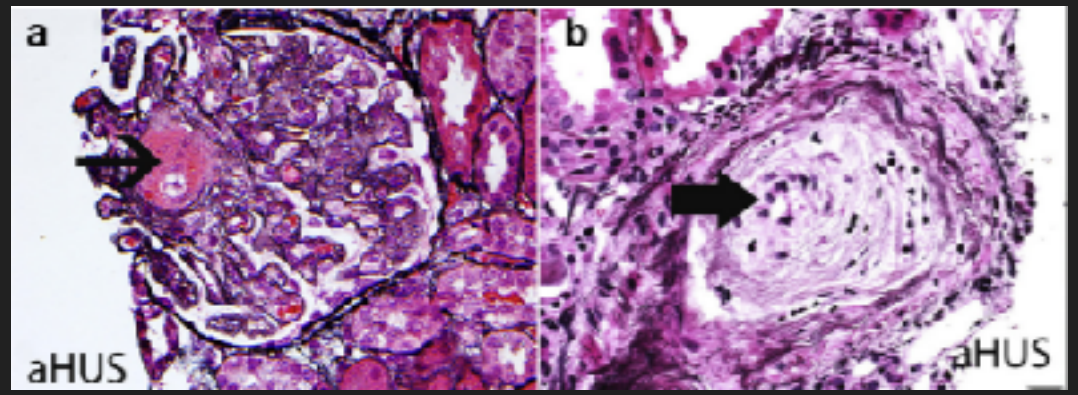
1. Loirat C, Frémeaux-Bacchi V. *Orphanet J Rare Dis*. 2011;6:60. 2. Dhaliwal G, et al. *Am Fam Physician*. 2004;69(11):2599-2606. 3. National Institute of Diabetes and Digestive and Kidney Diseases. Kidney failure: what to expect. https://www.niddk.nih.gov/-/media/0910262E529C436690C3112D89D8E1A3.ashx. Published December 2011. Accessed February 25, 2017. 4. Sellier-Leclerc AL, et al. *J Am Soc Nephrol*. 2007;18(8):2392-2400.

Thrombotic microangiopathies (TMA)

- TTP/HUS belong to a range of TMA and arises from an initial endothelial cell injury (vascular damage).

- Classic triad of HUS: non-immune thrombocytopenia, microangiopathic hemolytic anemia, and damage to various organs, predominantly the kidney and the brain *(in the setting of normal prothrombin time/PT and activated partial thromboplastin time/aPTT)*.

  ➢ Kidney pathology: **fibrin and platelet thrombi** in capillaries and arterioles, **endothelial cell swelling and detachment** from the glomerular basement membrane, and the appearance of so-called double contours on the glomerular basement membrane.



Fadi Fakhouri. Lancet 2017; 390: 681–96; Lilian Monteiro Pereira Palma. Kidney Int Rep (2021) 6, 11–23

Typical Haemolytic Uraemic Syndrome (HUS) and aHUS Have Different Pathophysiologies

- HUS comprises 2 types:
  - What was historically called *typical HUS* is caused by STEC and is now referred to as *STEC-HUS*[1]
    - It accounts for 90% of HUS cases[2]
    - Prognosis is usually good, with 80% of patients making a full clinical recovery and a mortality rate that is less than 5%[2]
  - Historically, HUS was referred to as *atypical* after STEC infection was excluded[1]
    - Prognosis is unfavorable[3,4]
      - 33% to 40% of patients develop end-stage renal disease (ESRD) or die during the first clinical manifestation of aHUS
      - 79% of patients die or progress to ESRD within 3 years of diagnosis

The pathophysiology of aHUS is now known to be caused by underlying **complement dysregulation**.[1]

1. Loirat C, Frémeaux-Bacchi V. *Orphanet J Rare Dis*. 2011;6:60. 2. Campistol JM, et al. *Nefrologia*. 2015;35(5):421-447. 3. Noris M, et al. *Clin J Am Soc Nephrol*. 2010;5(10):1844-1859. 4. Caprioli J, et al. *Blood*. 2006;108(4):1267-1279.

Unmet Medical Needs in Pediatric aHUS Kidney Transplant Patients

- Available drug (Eculizumab) within 24-48 hours following aHUS diagnosis, particularly for pediatric cases !

Early initiation of treatment (< 24–48 h) is highly recommended to stop TMA activity and to prevent chronic sequelae .

- In pediatric patients, treatment with eculizumab is the preferred option
- In adults, initial therapy with PE for 5 days is recommended.

Unmet Medical Needs in Pediatric aHUS Kidney Transplant Patients

- Available drug (Eculizumab) within 24-48 hours following aHUS diagnosis, particularly for pediatric cases !
- Flexible drug treatment policies give children a chance of receiving a kidney transplant.

罹患非典型溶血性尿毒症候群等待腎臟移植孩童需要及時和彈性的罕病用藥政策，贏得再次重生的機會和更美好的未來！

兒童案例 3

Neurodevelopmental outcome is effectively ameliorated by kidney transplantation in children at 6 years of age: Comparison of two cases

Mei-Ching Yu[a,*], Chao-Jan Wang[b], Yang-Jen Chiang[c]

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[b] Department of Radiology, Lin-Kou Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan
[c] Division of General Urology and Renal Transplantation, Lin-Kou Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taoyuan, Taiwan

已知慢性腎衰竭和末期腎病變對神經發育有不利影響兒科患者，特別是大腦正在發育的幼兒和幼兒（≤6 歲）。

我們報告兩名被診斷為末期腎臟病並在醫院接受自動腹膜透析的幼兒女孩年齡34個月。他們最初的大腦磁振造影顯示，主要小腦區域有腦部萎縮、腦室擴大和梗塞。他們兩人也都出現了癲癇發作。一名女孩接受了腎臟移植手術腹膜透析開始後4年進行移植。她的移植後神經影像顯示大腦結構不明顯的異常。此外，她沒有出現明顯的神經系統問題臨床上。相反，另一個尿毒症女孩則患有長期腦萎縮，無法控制癲癇和認知功能惡化。

從這兩個對比案例可以看出，腎臟移植可能是一種有利且有效的治療方法，可預防嚴重的神經發育障礙患有末期腎病的幼兒的殘

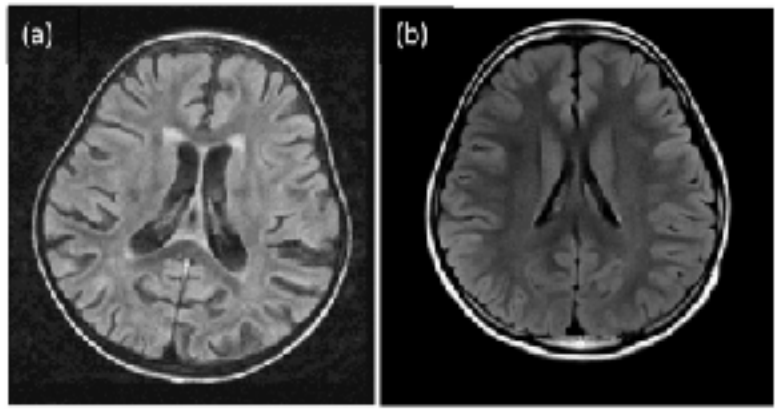


Fig. 1. A 34-month-old ESRD girl caused by bilateral renal hypodysplasia. Her initial MRI FLAIR T2 imaging of brain showed moderate ventricular dilatation and diffuse cortical atrophy (a). She received a deceased-donor kidney transplant at the age of 6 years. The follow-up MRI imaging of brain showed decreased ventricular size and significant improvement of cortical atrophy (b).

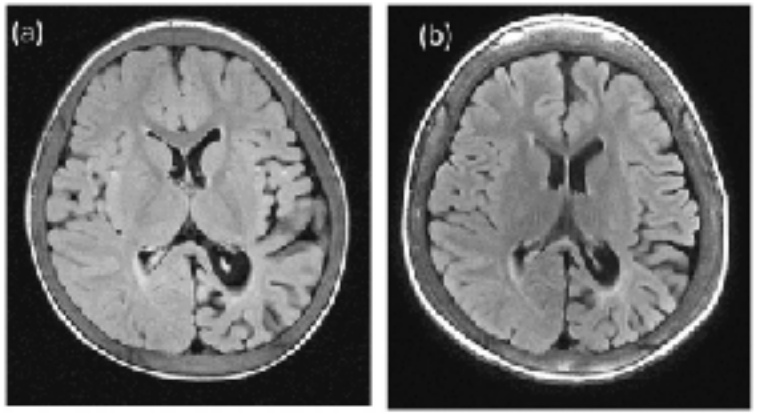
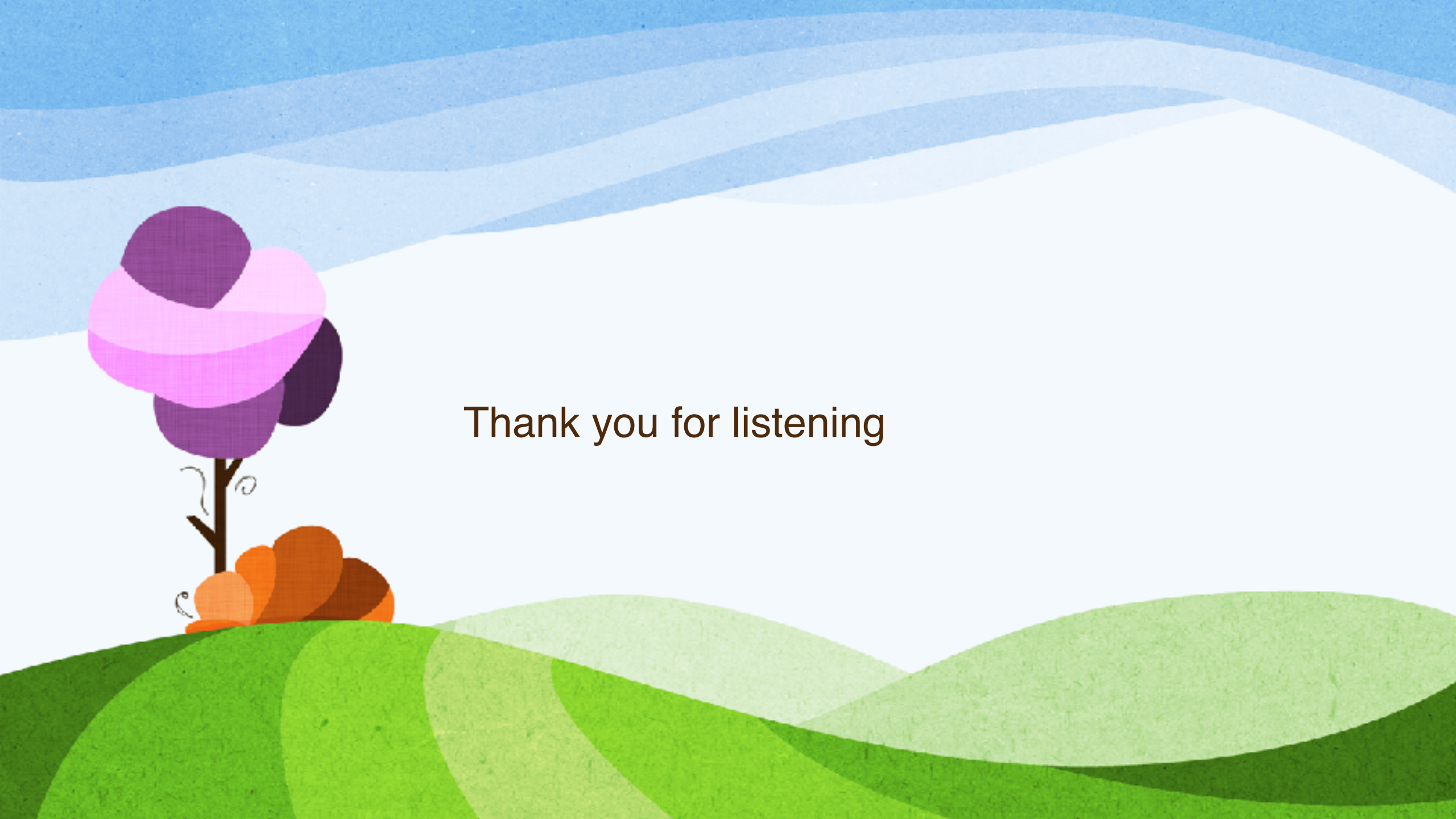


Fig. 2. A 34-month-old girl is diagnosed of ESRD secondary to crescentic GN. Her initial MRI FLAIR T2 imaging of brain showed asymmetric ventricular dilatation cortical atrophy, more severe on left side temporal, parietal and occipital lobes (a). Recently, the follow-up MRI shows no significant change of the ventricular dilatation and cortical atrophy (b).

慢性腎臟病孩童照護不同於成人病患, 需要團隊合力照護,陪伴這些孩子們勇敢面對未來。


Thank you for listening