# National Based, Retrospective Study on the Evaluation of Clinical, Laboratory, and Imaging Research of Tuberous Sclerosis Cases

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## INTRODUCTION

The aim of this study is to evaluate clinical, laboratory, and imaging studies of tuberous sclerosis complex (TSC) cases at the national level in Turkey.

## MATERIALS & METHODS

Patients who were diagnosed with TSC between January 2010 to January 2022 through a 23-centered retrospective study in Turkey and were followed up for at least 3 months, presenting complaints, demographic data, radiological findings, specific organ involvement, medical and surgical treatment options, response to treatment and follow-up.

## Results Table 1

| Signs and Symptoms | N | % of All | Age at onset/ Mean ±SD | Median (min-max) | *p* |
|---|---|---|---|---|---|
| The first application to the hospital | 774 | 100 | 42.6±49.4 | 18/6-72 | <0.01 |
| Gender(F/M) | 355/ 419 | 45.8/ 54. 2 | - | | |
| Application Complaint | | | | | |
| Seizure | 544 | 70.2 | | | |
| Skin Signs | 90 | 11.6 | | | |
| Learning Difficulty | 4 | 0.51 | | | |
| Psychiatric Symptoms | 2 | 0.25 | | | |
| The Others(rhabdomyoma/ Incidentally ect) | 134 | 17.3 | | | |
| Neurologycal findings | 650 | 83.97 | | | |
| Epilepsy | 640 | 82.68 | | | |
| West Syndrome *(*99 cases disappeared)* | 223 | 28.81 | 7.5±8.5 *Disappear 24.5±25.2 | 6/3-8.2 *Disappear 14/7-144 | <0.01 |
| Focal Seizures* *(*92 cases disappeared)* | 374 | 48.3 | 25.9±34.7 *Disappear 68.3±54.9 | 12/0-204 *Disappear 60/0-245 | <0.01 |
| Generalized Seizures* *(*93 cases disapperared)* | 379 | 48.9 | 26.6±37.6 *Disappear 47±48 | 11/0-240 *Disappear 24/1-216 | <0.01 |
| LGS* *(*one case disapperared)* | 43 | 5.5 | 50.3±30.4 *Disappear 66 | 41/11-120 | - |

## Results Table 2

| Signs and Symptoms | N | % of All | Age at onset/ Mean ±SD | Median (min-max) | *p* |
|---|---|---|---|---|---|
| TAND | 651 | 90.4 | | | |
| Anksiety | 81 | 10.4 | | | |
| İntellectuel Disability | 642 | 82.9 | - | | |
| Border zone/ mild | 489 | 63.1 | - | | |
| Moderate | 98 | 12.6 | - | | |
| Severe | 55 | 7.1 | - | | |
| Autism Spectrum Disorder | 126 | 16.2 | 30.8±24.3 | 36(24-101) | <0.01 |
| ADHD | 119 | 15.3 | 58.2±28.8 | 54.5(48-160) | 0.09 |
| Mood Disorders | 44 | 5.6 | 85.5±64.9 | 60(24-216) | 0.06 |
| Depression | 12 | 1.55 | - | - | |
| Decreased Self Esteem | 8 | 1.03 | - | | |
| Other(disartri,aggressive excited, puberty and adjustment disorder | 19 | 2.4 | - | | |
| MRI used | 761 | 98.3 | | | |
| Cortical Tubers /Hamartomas | 652 | 84.2 | 38.46±48 | 13.5/5-60.5 | |
| SENs | 505 | 65.3 | 39.9±47.9 | 16/6-60 | |
| Lineer White matter Lesions/ Heterotopia | 114 | 14.7 | 51±51.2 | 30(0-216) | <0.01 |
| SEGA | 110 | 14.2 | 67.9±59.8 | 60/12.2-120 | |
| Hypomyelination areas | 57 | 7.3 | - | - | |

## RESULTS

Totaly 774 patients were included, newborns to 18 years, mean age at onset was 42.6 months with 74 months follow-up time. 70.2% presented with epilepsy, %11.6 with only skin lesions, 0.3% with learning problems, and %17.9 with other problems.

Hypomelanotic macule and ash leaf were detected in the most of skin lesions (631- 81.5 % of all patients) then respectively comes anjiofibromas, shagreen patches, confetti-like macules, periungual fibroids, molluscum fibrosum and other fibrous lesions. Renal Angiomiyolipomas was detected about 32% and 185/250 of them were bilateral; Renal cysts were only at 14.8% and frequently unilateral(85/115)

82% of total cases (n:640) had epilepsy with a mean onset of 22 months and 213/640 were followed up with West syndrome. Intellectual disability was 87.3% (40.1% borderline, 25.5% mild, 13.4% moderate, 6% severe and 1.4% very severe). Autism spectrum disorder 14 % (100/714) and attention deficit hyperactivity disorder 14.1%(101/714) were not rare.

There was a positive and statistically significiant correlation between age at onset and beginning age of epilepsy r=0.47,p<0,01

Also beginning age of SENs –SEGA and Cortical Tubers with beginning age of epilepsy had a positive and statistically significant correlation (respectively r:0.62-0.59-0.62, p<0,01)There was negative correlation between mTOR dose and Vigabatrin dose (r:-0.75,p:0,05) and mTOR dose with Vigabatrin using the time(r:-0,64, p:0,082)

Between Vigabatrin dose and vigabatrin using time was also negative correlated.(r=-0.149, p:0,033)

## Results Table 3

| Signs and Symptoms | N | % of All | Mean ±SD | Median (min-max) |
|---|---|---|---|---|
| Treatment | 658 | 85 | - | - |
| Antiepileptic (VPA/LEV/TPX/CMZ vs) | 645 | 83.3 | - | - |
| Vigabatrin | 399 | 51.5 | Time:30.1±30.6 Dose:94.3±33.5 | Time:24 (8-36) Dose:100 (70-120) |
| Everolimus | 91 | 11.7 | - | - |
| Antipsychotic | 60 | 7.7 | - | - |
| ACTH | 58 | 7.5 | - | - |
| Sirolimus | 42 | 5.4 | - | - |
| Surgery | 46 | 5.9 | - | - |
| Piridoksin | 19 | 2.4 | - | - |
| mTor* Time(Months) mTor*Dose(mg/m²) | *39 | 5 | Time:26±23.6 Dose:3±1.15 | Time: 24/2-96 Dose: 2.5/2-5 |
| Following patients | 613 | 79.2 | - | - |
| Follow-up time * | 754 | | 74±60.72 | 60/1-390 |
| Mortality | 31 | 4 | - | - |

## CONCLUSIONS

TSC is a complex disorder that is associated with many organs and systems. Skin examination is important to suspect TSC. In this study, it was observed that the frequency of cranial involvement at the time of admission was high and the first admission was after serious complaints such as seizures. For this reason, prospective studies with large case series and epidemiology studies are needed.

The retrospective study had some difficulties to reach some records( for example time to the beginning of signs and symptoms and the resolution time, drugs dose and duration of use, the dimensions of lesions before and after the surgery)

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