

Fungiuria: Laboratory-Based 08-Year Analysis in paediatric age group at C.N.B.C and M.Y.H -A Tertiary care hospitals of MGMMC, Indore M.P

Dr.S.S.Thakur¹ Dr.Priya Patel² Dr.Chakshu sukheja³ Dr.Mohammad Wasif Manzoor⁴ Dr.Sunil Kumar⁵ Dr.Meena Mittal⁶ Dr.Ashok Panchonia⁷

(Associate Professor,MGM Medical college,indore)

(Resident medical officer,MGM Medical college,indore)

(Resident medical officer,MGM Medical college,indore)

(Resident medical officer,MGM Medical college,indore)

(Resident medical officer,MGM Medical college,indore)

(Professor,MGM Medical college,indore)

(Professor,MGM Medical college,indore)

Abstract

Fungiuria or in simple way Fungal urinary tract infection (UTI) represents a common cause for urinary tract infection in paediatric age group. Since few years , increasing incidence is associated with long and high dose use of broad-spectrum antibiotics, steroids, immunosuppressive and cytotoxic drugs. Other contributing factors include congenital structural or functional abnormalities of urinary tract with indwelling urinary catheter .Since the pandemic of SARS-CoV-2, a significant rise in threatening fungal co-infections in COVID-19 patients has been testified in the scientific literature. all urine sample submitted in OPD and IPD of symptomatic patients with fungiuria of $>10_{4-5}$ CFU/ml and leucocyturia were analysed for etiology, risk factors and outcome. Candida albicans was isolated in maximum number of paediatric population and non-Candida yeasts (aspergillous species)observed in few cases. Based on microscopic fungal hyphae score and clinical symptoms ,they were treated with systemic antifungals. Systemic antifungal therapy should be considered in high-risk patients with age group 1-4yr along with high fungal score (FH++++).

Introduction

The incidence of candiduria and fungal urinary tract infections (UTI) has increased in recent years. Risk factors comprise the extensive use of broad-spectrum antimicrobial agents, corticosteroids, immunosuppressive agents, cytotoxic chemotherapy complicated by mucositis and neutropenia, elderly age, diabetes mellitus, structural or functional abnormalities of urinary tract with indwelling urinary catheter or nephrostomy. Increased incidence is also observed in chronic renal failure and hemodialysis patients. Renal transplant patients are at high risk for developing funguria and pyelonephritis due to immunosuppressive therapy [1], [2], [3].

The most frequent organism causing fungal UTI is still *Candida albicans* followed by *Candida (Torulopsis) glabrata*, *Candida tropicalis*, and *Candida krusei* [1], [4]. Non-*albicans* *Candida* and non-*Candida* yeasts are steadily increasing as the etiological cause of fungal UTI [4]. In comparison with bacterial UTI, the diagnostic criteria of significant funguria and fungal UTI are not well established. Wise et al. [5] concluded that an increased risk of fungal pyelonephritis was associated with counts of greater than 15 000 CFU/ml. Other authors [6], [7] defined the cut-off between colonization and infection as the lowest colony count from a single urine specimen to be 10⁵ CFU/ml of fungal pathogen. In 5–15% of patients with symptomatic fungal UTI, funguria is accompanied by fungemia [4]. We aimed to analyze the trends of frequency, distribution of fungal hyphae isolated from urine routine microscopy of both ambulatory patients and inpatients in this study.

Objectives

1. The purpose of this study was to determine the prevalence of fungiuria in paediatric age group from year 2015 to 2022 in M.Y.H and C.N.B.C,Indore .
2. To study the association of age and fungiuria from year 2015 to 2022
3. To know the association of covid-19 and fungiuria in paediatric age group.

Material and methods

A total of average 2500 urine sample of patients submitted every year in MY Hospital between age group of neopnates to 15 years retrospectively. in the years 2015–2022 with suspected UTI were analysed . There were about 1350 males and 1150 females with a mean age of 4- 5 years. Inclusion criteria were microscopic documentation of funguria , leucocyturia (>10/HPF×400), fever >38°C and typical symptoms of UTI (dysuria, frequent urination, lumbar pain or tenderness, etc.).

All urine sample,minimum 12-15 ml collected in clean ,sterilised,flat bottom transparent container .followed by centrifugation at 1500 rpm for 5 min .supernatant discarded and sediment analysed , preparing wet mount preparation.Budding yeast and hyphae in urine were identified under high power magnification of compound microscope followed by further confirmation made by allowing culture of fungal hyphae.

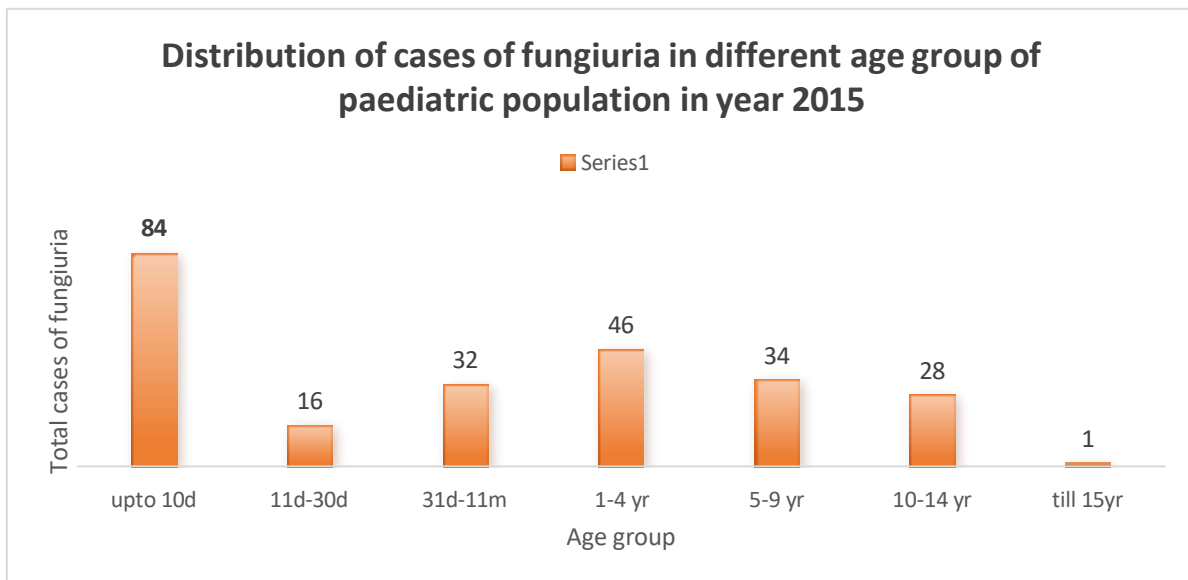
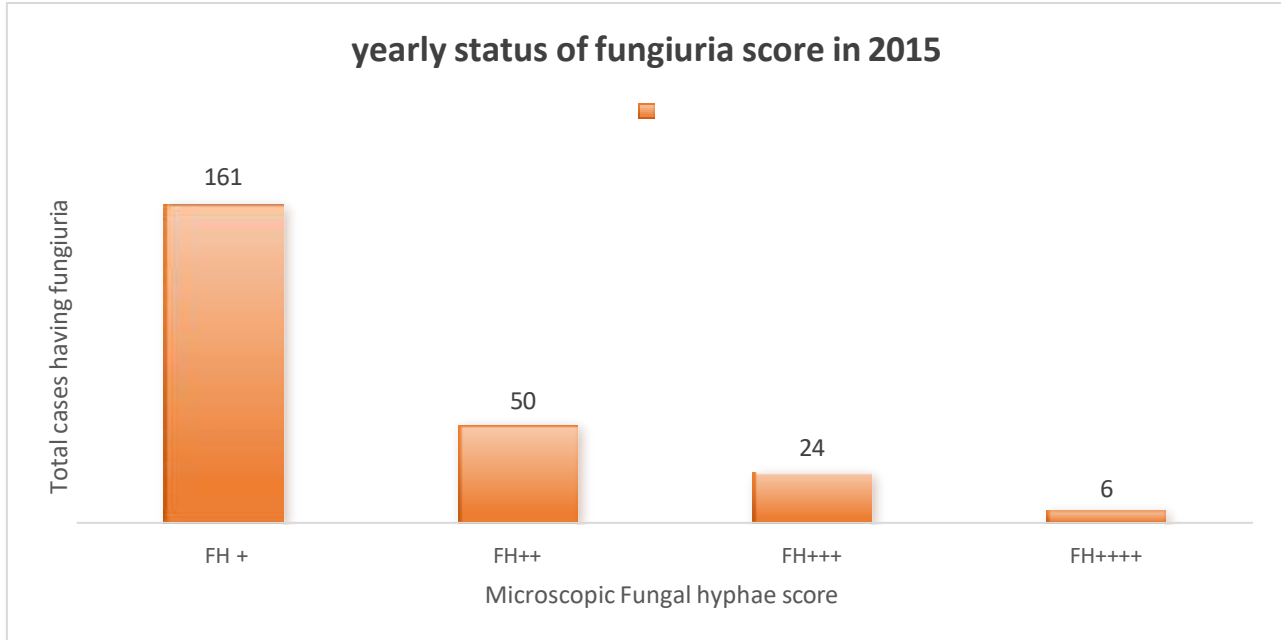
Results and Observation

Fungiuria especially candida in the urine is a potentially lethal pathogen.their early identification provide window for management of an average of 250 paediatric patient every year.Urine colony counts and clinical observations determine therapy.The most frequent risk factors associated with the development of symptomatic fungal UTI based on

clinical details and hematological findings were: antibiotic therapy with more than one agent in the previous 7 days (96%), previous long-term or high-dose steroid therapy (72%), concurrent fungal infection or colonization at a site other than the urinary tract (48%), presence of an indwelling urinary catheter or nephrostomy tube (46%), hematological malignancies with neutropenia (30%), pancytopenia, structural or anatomical abnormalities of the urinary tract (26%), and diabetes mellitus (12%). Significant differences in distribution of fungal hyphae were observed based on age and yearly status of last 8 years from 2015 to 2022. where patients were treated, including ambulatory care, inpatient units, and intensive care units.

YEAR 2015

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	48	21	10	5	84
11d -30 d	11	2	3	-	16
31d-11m	20	7	5	-	32
1yr-4yrs	33	9	4	-	46
5yrs-9yrs	27	6	1	-	34
10yrs-14yrs	21	5	1	1	28
Till 15yrs	1	-	-	-	1
Total	161	50	24	6	241

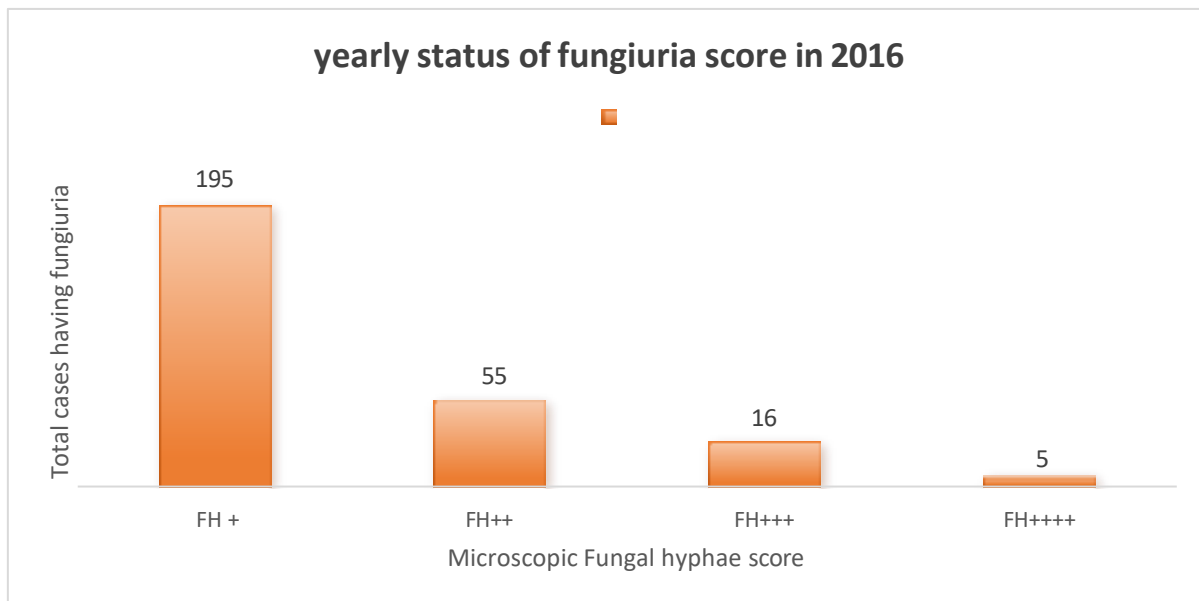


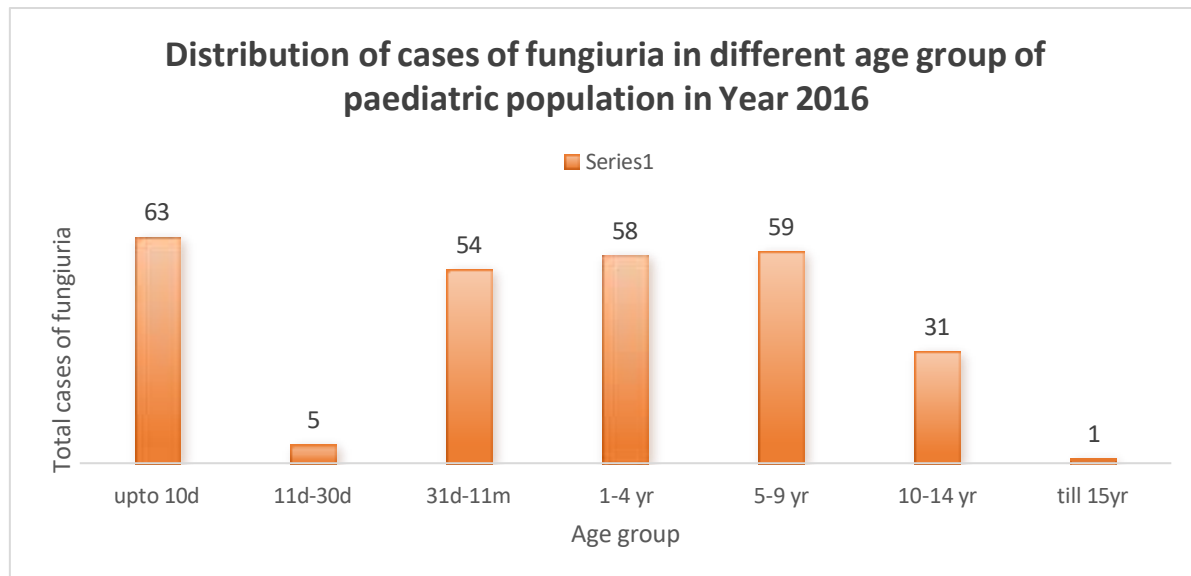
Year 2015 data relates with highest susceptibility rates for fungiuria observed age group ,upto 10 d (84 out of 241 total fungiuria cases)with highest interpretation of FH+ followed by FH ++ .

FH++++ reported cases were being least in number(6 out of 241 total fungiuria cases) that too maximum reported in age group upto 10 d (5 out of 6 FH++++ cases).

YEAR 2016

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	45	11	6	1	63
11d -30 d	3	-	1	1	5
31d-11m	37	13	3	1	54
1yr-4yrs	40	12	5	1	58
5yrs-9yrs	44	14	1	-	59
10yrs-14yrs	26	5	-	-	31
Till 15yrs	0	-	-	1	1
Total	195	55	16	5	271



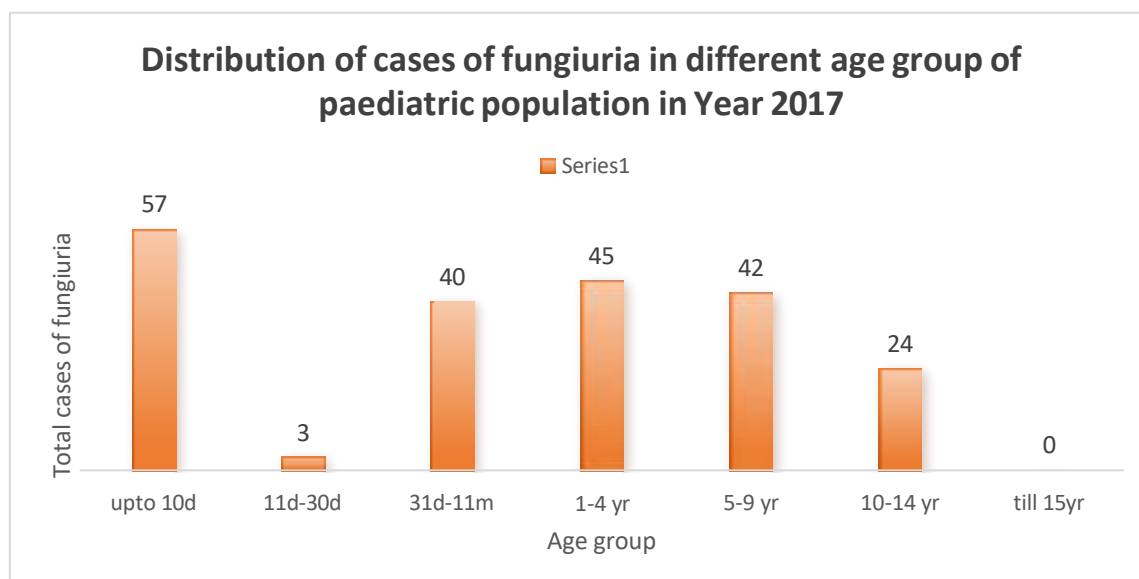
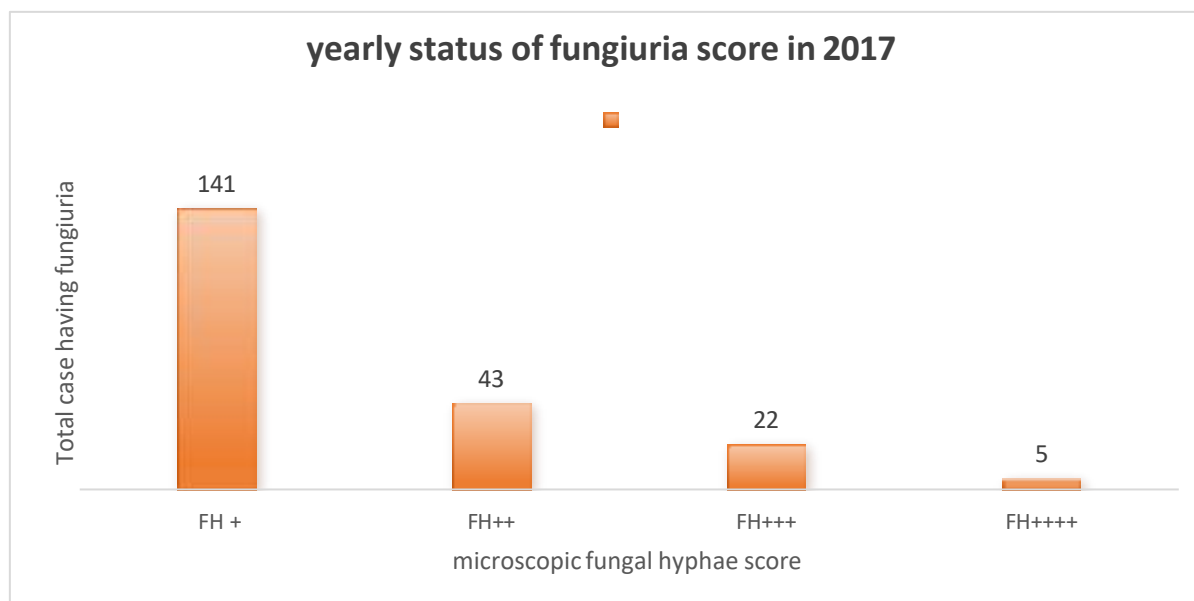


Year 2016 data relates with highest susceptibility rates for funguria observed age group ,upto 10 d (63 out of 271 total funguria cases)with highest interpretation of FH+ followed by FH ++ .

FH++++ reported cases were being least in number(5 out of 271 total funguria cases) that is equally distributed among age group upto 10 d to till 15y.

YEAR 2017

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	37	12	6	2	57
11d -30 d	2	-	1	0	3
31d-11m	26	9	5	0	40
1yr-4yrs	32	8	4	1	45
5yrs-9yrs	29	8	3	2	42
10yrs-14yrs	15	6	3	-	24
Till 15yrs	-	-	-	-	-
Total	141	43	22	5	211

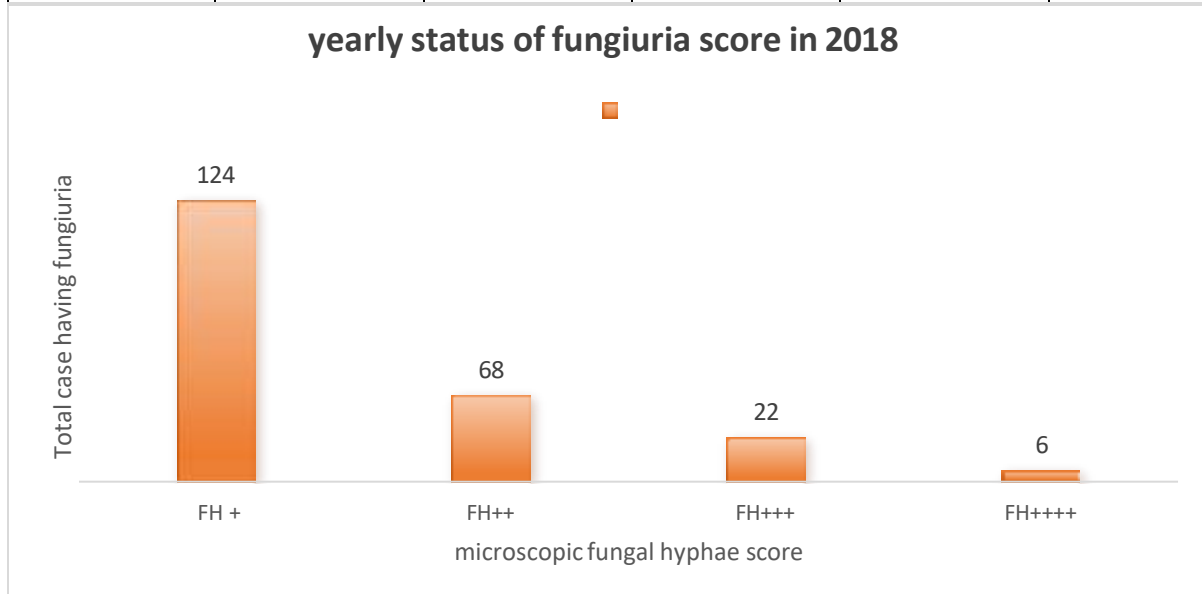


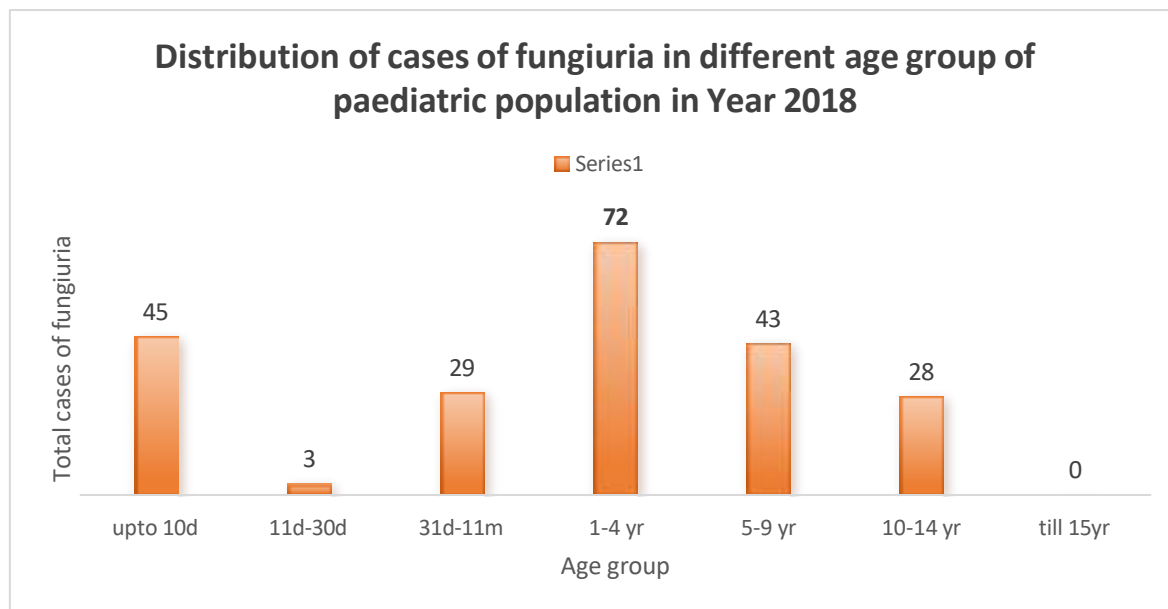
Year 2017 data relates with highest susceptibility rates for fungiuria observed age group ,upto 10 d (57 out of 211 total fungiuria cases)with highest interpretation of FH+ (141 out of 211 total fungiuria cases)followed by FH ++(43 out of 211 total fungiuria cases) .

FH++++ reported cases were being least in number(5 out of 271 total fungiuria cases) .

YEAR 2018

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	20	17	7	1	45
11d -30 d	1	2	-	-	3
31d-11m	18	8	3	-	29
1yr-4yrs	48	15	8	1	72
5yrs-9yrs	24	16	1	2	43
10yrs-14yrs	13	10	3	2	28
Till 15yrs	-	-	-	-	-
Total	124	68	22	6	220



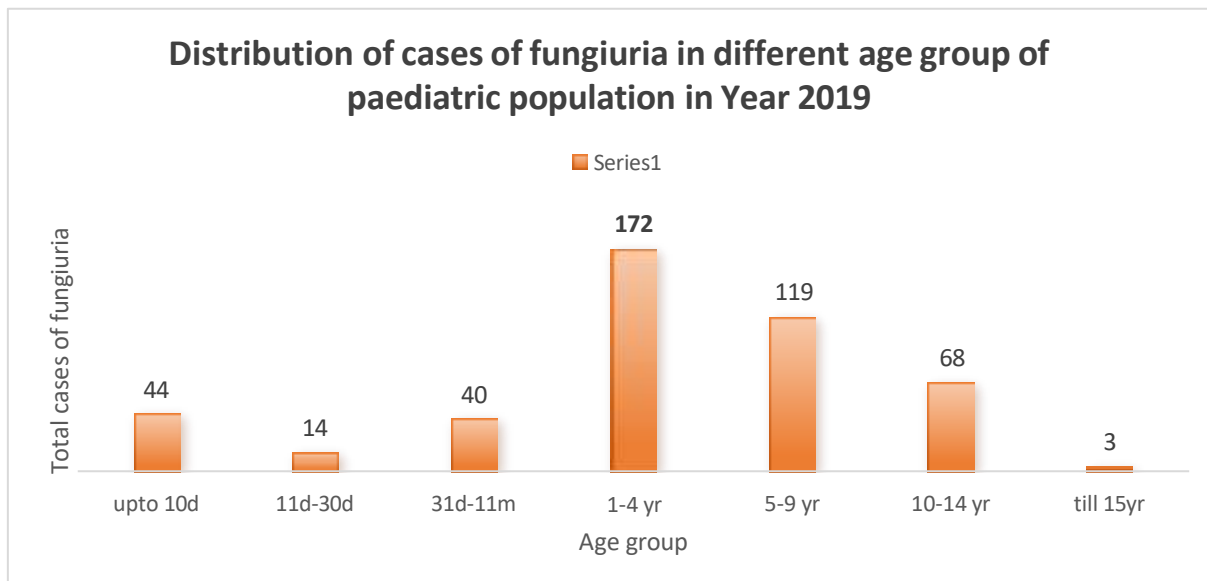
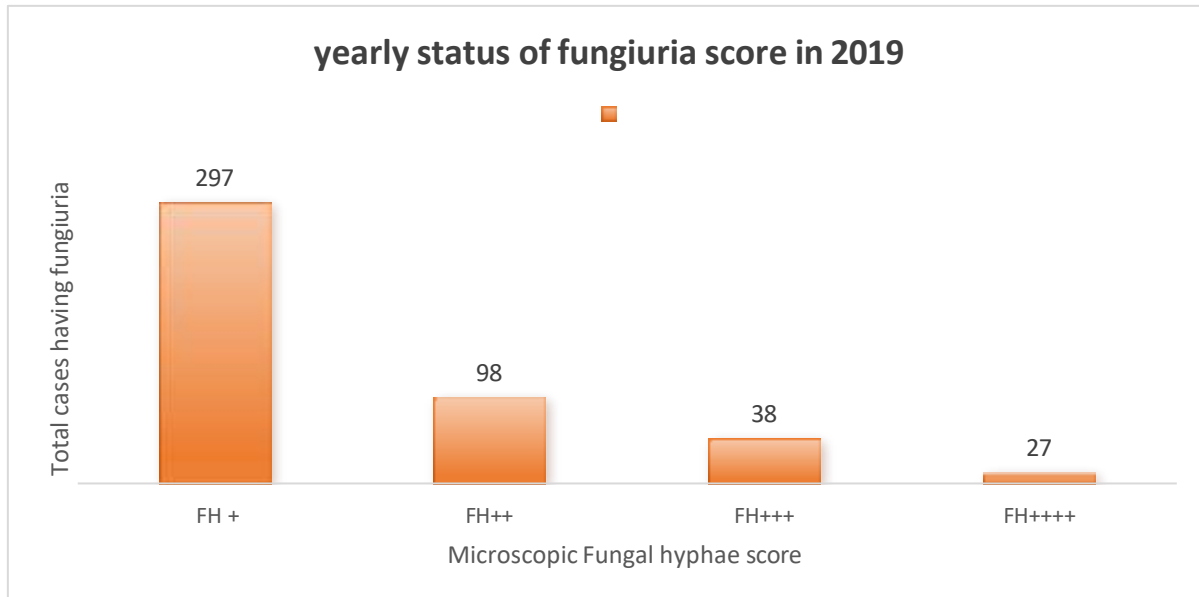


In contrast to last 3 years, Year **2018** data relates with highest susceptibility rates for fungiuria observed age group, **1-4 yr** (72 out of 220 total fungiuria cases) with highest interpretation of FH+ (48 out of 220 total fungiuria cases) followed by FH ++ (15 out of 220 total fungiuria cases) .

FH++++ reported cases were being least in number (6 out of 220 total fungiuria cases) .

YEAR 2019

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	26	12	3	3	44
11d -30 d	7	2	4	1	14
31d-11m	26	6	2	6	40
1yr-4yrs	113	41	12	6	172
5yrs-9yrs	80	20	11	8	119
10yrs-14yrs	43	16	6	3	68
Till 15yrs	2	1	-	-	3
Total	297	98	38	27	460

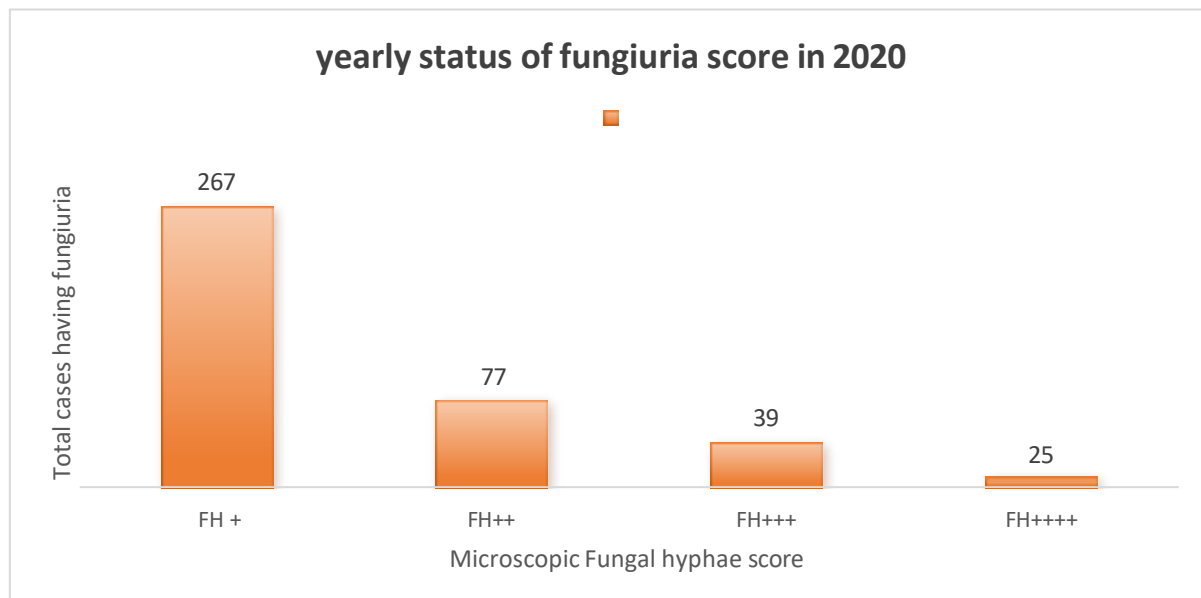


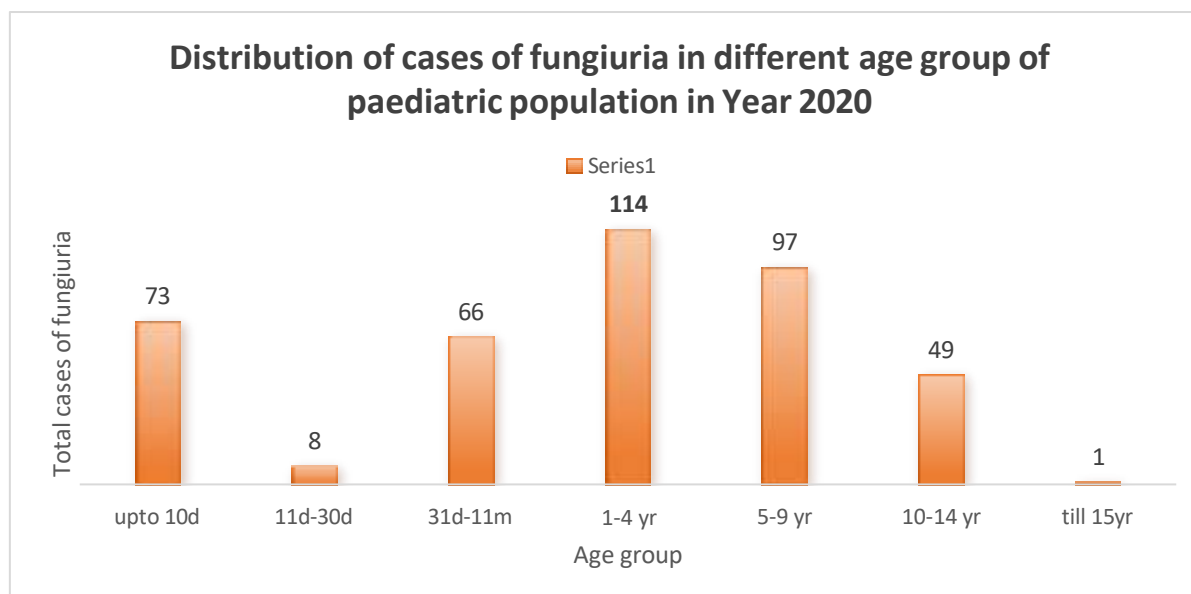
In year 2019 there is a significant increase in total fungiuria cases (Total 460 cases) .Similar to last year 2018 , **2019** data relates with correlated with highest susceptibility rates for fungiuria observed age group ,**1-4 yr**(172 out of 460 total fungiuria cases)with highest interpretation of FH+(113 out of 460 total fungiuria cases)followed by FH ++(41 out of 460 total fungiuria cases)

FH++++ reported cases were being least in number(27 out of 460 total fungiuria cases) .

YEAR 2020

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	39	16	10	8	73
11d -30 d	4	2	1	1	8
31d-11m	44	11	6	5	66
1yr-4yrs	79	23	8	4	114
5yrs-9yrs	67	18	7	5	97
10yrs-14yrs	33	7	7	2	49
Till 15yrs	1	-	-	-	1
Total	267	77	39	25	408

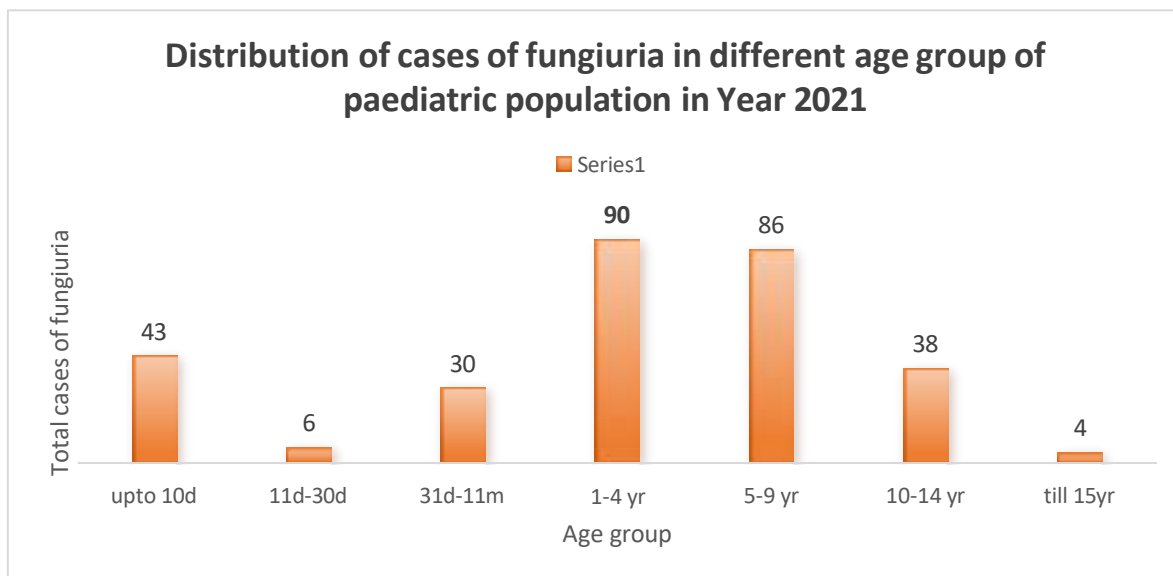
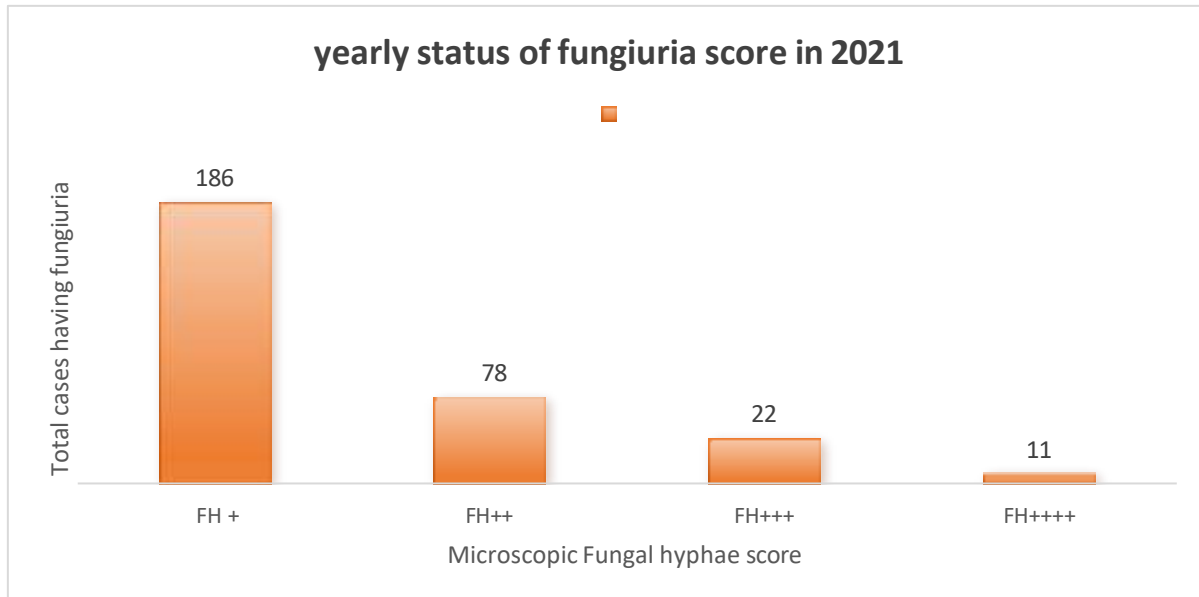




Like last year 2019, There is a significant increase in total fungiuria cases (Total 408 cases) Similar to year 2018, **2020** data relates with correlated with highest susceptibility rates for fungiuria observed age group, **1-4 yr** (114 out of 408 total fungiuria cases) with highest interpretation of FH+ (79 out of 408 total fungiuria cases) followed by FH++ (23 out of 408 total fungiuria cases) FH+++ reported cases were being least in number (25 out of 408 total fungiuria cases).

YEAR 2021

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	21	10	6	6	43
11d -30 d	1	4	1	-	6
31d-11m	17	10	2	1	30
1yr-4yrs	59	23	5	3	90
5yrs-9yrs	60	19	6	1	86
10yrs-14yrs	26	10	2	-	38
Till 15yrs	2	2	-	-	4
Total	186	78	22	11	297



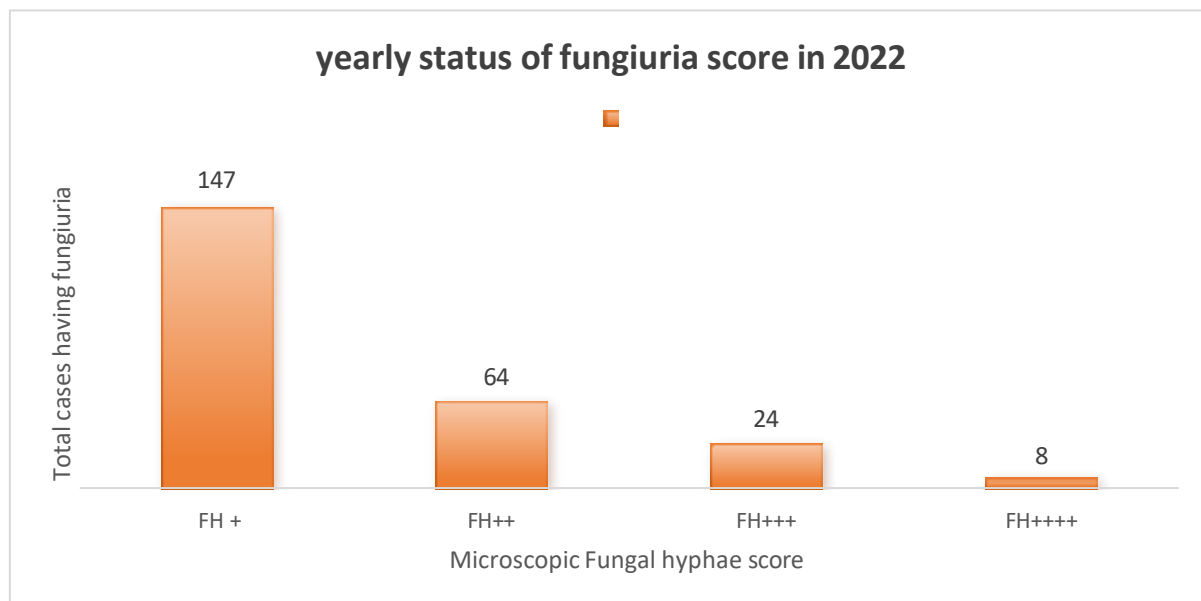
In contrast to year 2019 -2020 data, there is reduction in fungiuria case (Total cases-297),

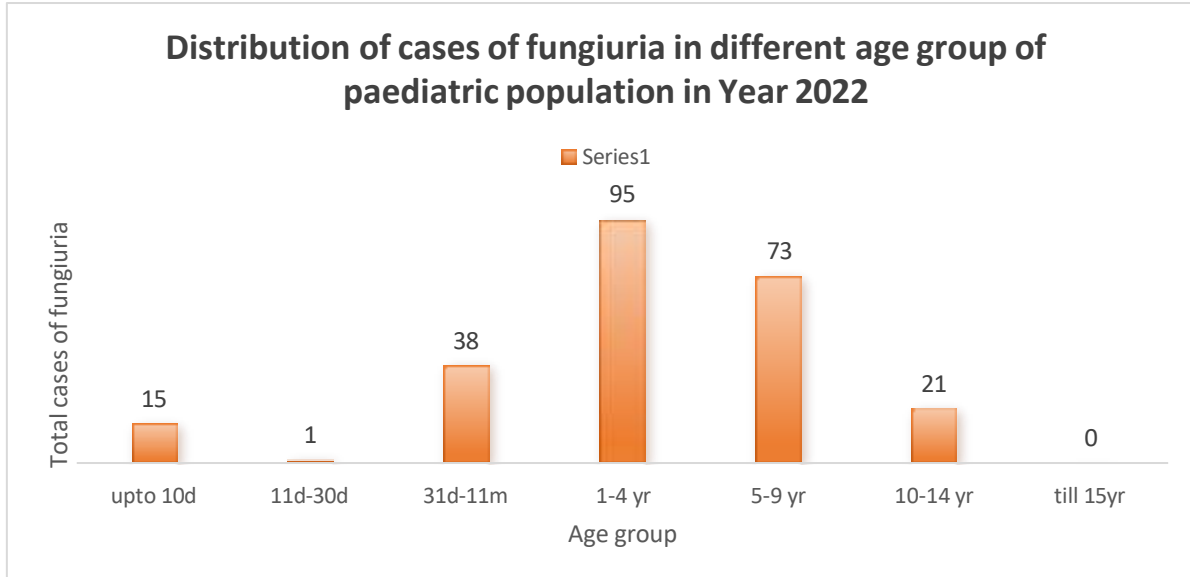
Similar to year 2018 , **2021** data relates with correlated with highest susceptibility rates for fungiuria observed age group ,**1-4 yr**(90 out of 297 total fungiuria cases)with highest interpretation of FH+(59 out of 297 total fungiuria cases)followed by FH ++(23 out of 297 total fungiuria cases)

FH++++ reported cases were being least in number(11 out of 297 total fungiuria cases) .

YEAR 2022

Age	Fungal hyphae +	Fungal hyphae ++	Fungal hyphae +++	Fungal hyphae ++++	Total
upto 10 d	11	1	2	1	15
11d -30 d	-	-	-	1	1
31d-11m	20	8	7	3	38
1yr-4yrs	65	22	7	1	95
5yrs-9yrs	40	26	5	2	73
10yrs-14yrs	11	7	3	-	21
Till 15yrs	-	-	-	-	-
Total	147	64	24	8	243

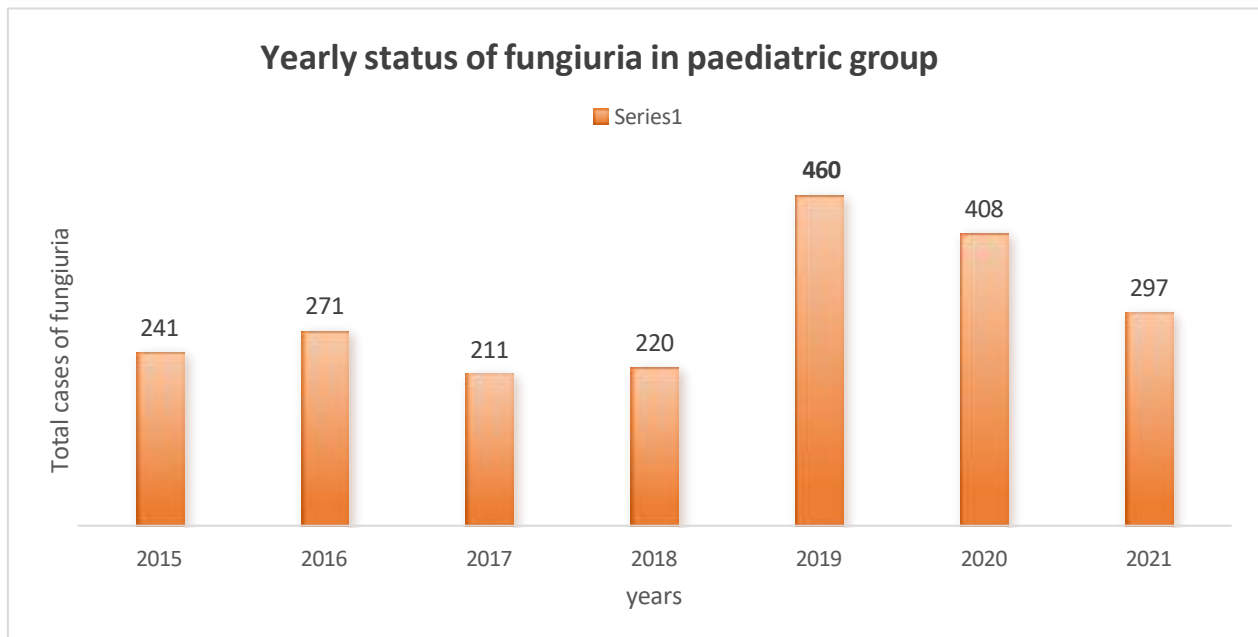




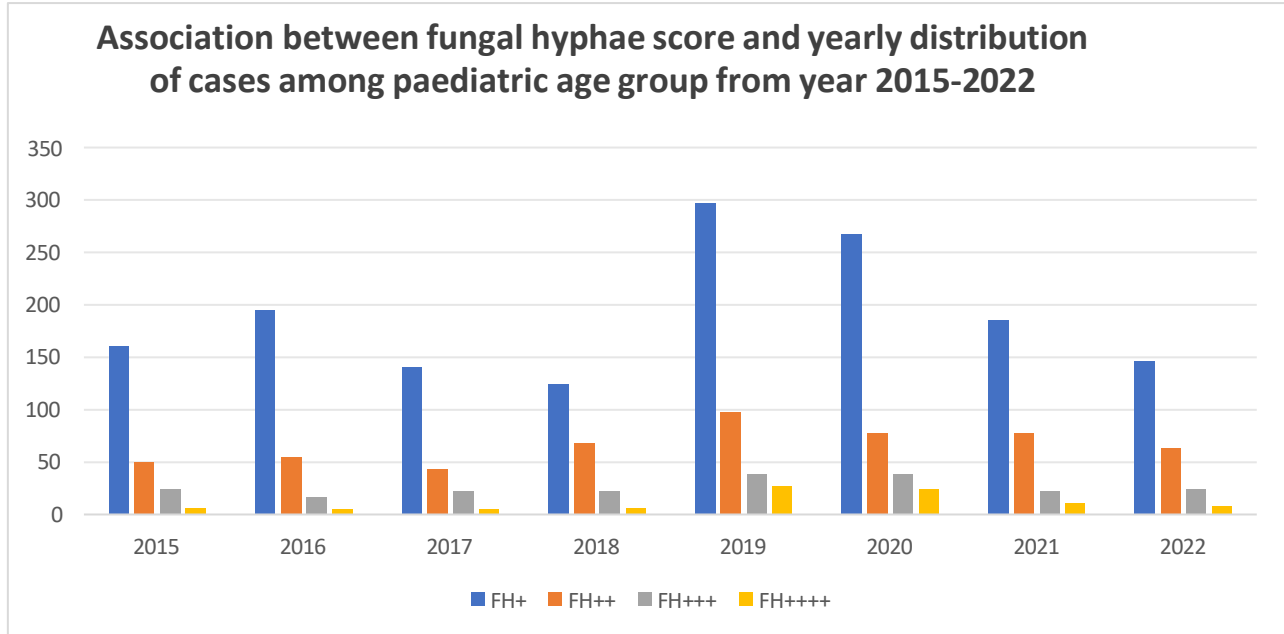
In contrast to year 2019 -2020 data,there is still more reduction in fungiuria case (Total cases-243)relative to year 2021.Similar to year 2018 , **2022** data relates with corelated with highest susceptibility rates for fungiuria observed age group ,**1-4 yr**(95 out of 243 total fungiuria cases)with highest interpretation of FH+(65 out of 243 total fungiuria cases)followed by FH ++(22out of 243 total fungiuria cases)

FH++++ reported cases were being least in number(8 out of 243 total fungiuria cases) .

Yearly status 2015-2022	Total case having fungiuria
2015	241
2016	271
2017	211
2018	220
2019	460
2020	408
2021	297
2022	243
Total	2351



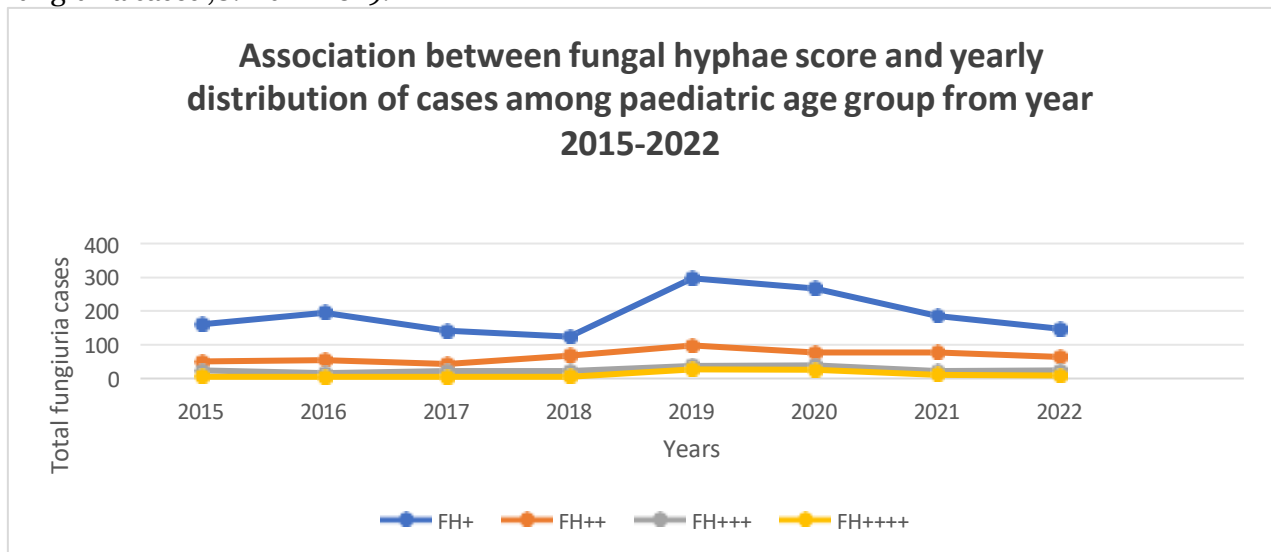
Total about 2351 fungiuria cases reported in 8 year analysis of laboratory data. The susceptibility of fungiuria prominent increased (from 9.6% to 18.4%) from year 2015 to 2019 respectively. A decrease was observed in the UTI against fungiuria in years 2020 then further more decreased in 2021; from 18.4% (2019 yr) to 16.0 % (2020 yr) then to 11.0% (2022 yr).

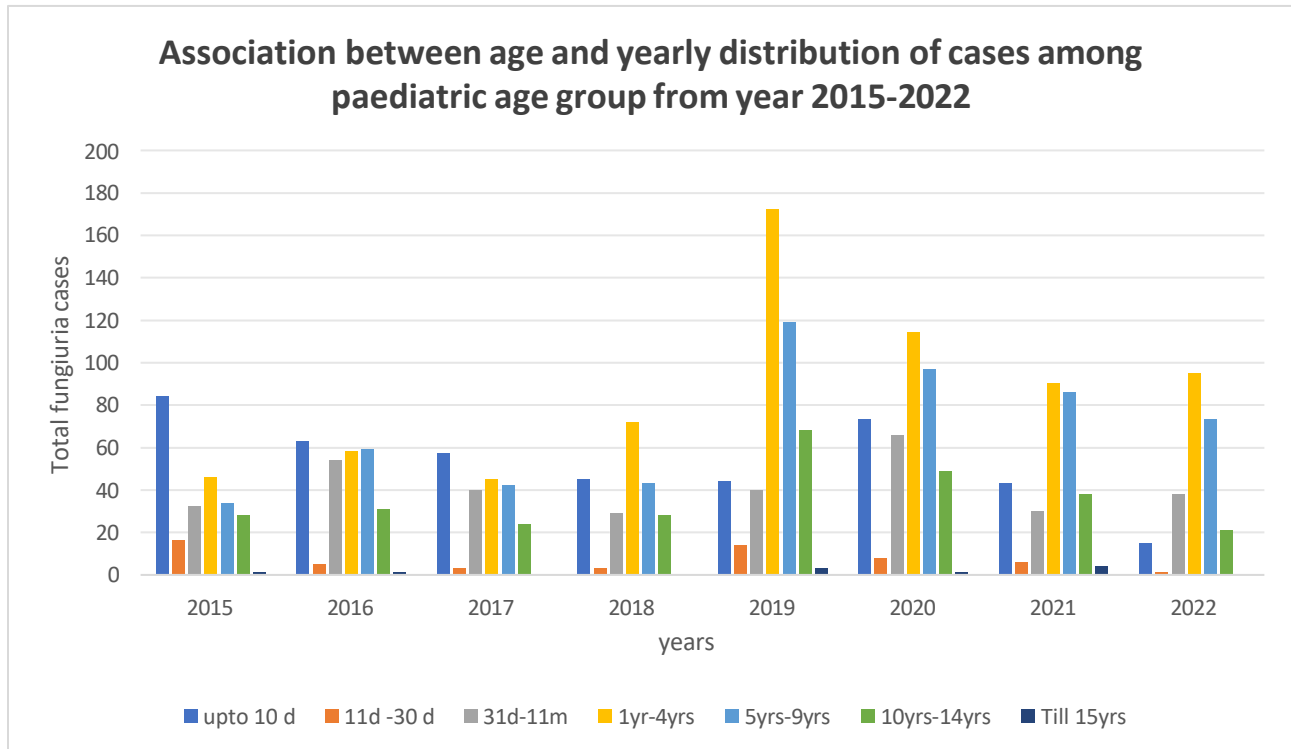


Fungal hyphae score (FH++++) 5.8% also has been significantly increased in 2019 (FH++++: 27 out of 460 total fungiuria cases) in year 2020, 6.12% (25 out of 408 total fungiuria cases), relative to year 2015, 2.48% (FH++++ : 6 out of 241 total fungiuria cases)

With subsequent years followed by pandemic 2019-20, there is decrease in prevalence of fungiuria cases along with fungal hyphae score. As noted in above bar diagram 2021, 3.7% (11 out of 297 total fungiuria cases), and 2022, 3.29% (8 out of 243 total fungiuria cases).

There has been steadily rise in total number of cases of F+++ score from 2015 to 2019 but no significant changes seen when compared with percentage; 24 out of 241 total fungiuria cases, 9.9% in 2015; 55 out of 271 total fungiuria cases, 20.0% in 2016; 22 out of 241 total fungiuria cases, 9.12% in 2017; 22 out of 220 total fungiuria cases, 10.0% in 2018; 38 out of 460 total fungiuria cases, 8.2% in 2019.





In contrast to prevalence of funguria cases among age group -upto 10d(34.8%) in year 2015, we have noted there is significant increase in prevalence of funguria cases in age group 1-4 yr in year 2019(37.3%), followed by decrease in distribution of cases among this group in year 2020(27.9%) then rise in cases in year 2021(30.3%) and 2022(39.0%).

Images



Fig 1.-Interpretation -Candida species FH++++ (high power magnification)

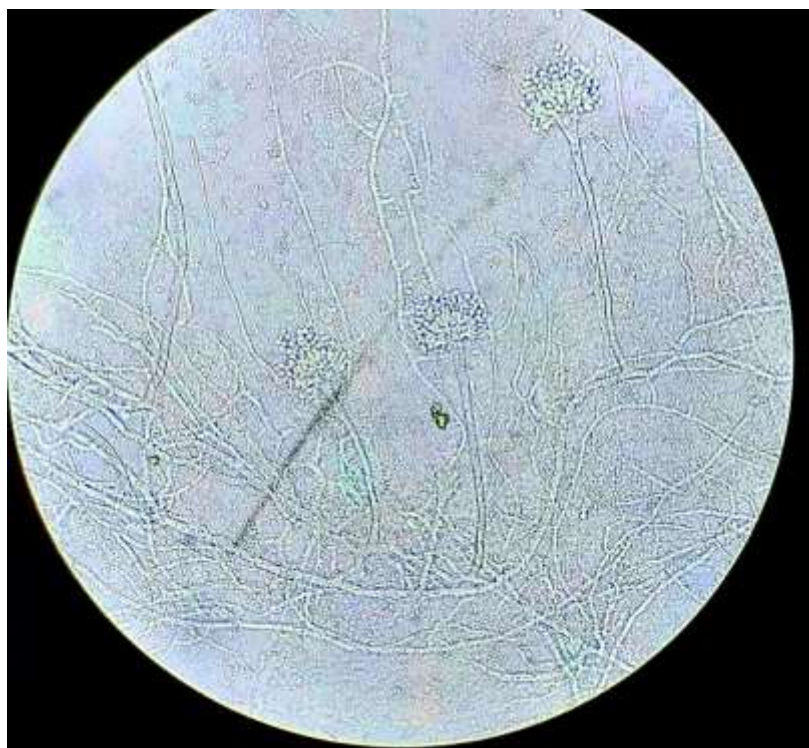


Fig 2.Interpretation -Aspergillous species FH++++ (high power magnification)

Discussion

Based on various previous article, symptomatic fungal UTI require therapy . Past literature gave evidence of Cases of fungal pyelonephritis [8], papillary necrosis [9] and fungal bezoar formation [10] .Asymptomatic funguria was treated if found in high-risk patients, such as those with renal transplants, obstructive uropathy, neutropenia, type 1 diabetes mellitus, or other immunocompromised conditions. [1], [3].

Bladder irrigation with antifungal drugs is recommended in cases involving non-cooperative pediatric patients or when catheter removal is not feasible.

Previous study reported the lower urinary tract symptoms may be one of the early symptoms of COVID-19 infection ([10](#)).Increased age was also found to increase the incidence of lower urinary tract symptoms ([12](#)). However, in 57 patients, seven patients experienced urinary frequency symptoms as one of the symptoms of COVID-19 ([13](#)).In our study we found significant increase in fungiuria cases among more older group 1-4 yr in 2019 as compared to year 2015 age group -upto 10 d.their percentage quite similar in subsequent year with slight fluctuation of percentage in distribution of cases.

Incontrast to most common species of candida(fig-1) in urine ,we have reported o1,a rare case of aspergillous species(FH ++++)(fig-2) in pediatric age group in year 2019 with significant history of fever ,lower lumber pain and leucocyturia ,rt-pcr covid positive.

Also we have reported significant decrease in fungiuria case in 2021 and 2022,it correlates how much the influence of COVID-19 symptoms had with lower urinary tract fungiuria .This study show the significant association of fungiuria with covid19 pandemic.9.6% in 2015 to 18% in 2019.The high association of COVID-19 on lower urinary tract fungiuria is due to infection of yeast hyphe in immunocompromised paediatric age group. Inflammation causes damage to the bladder mucosa; this damage results in lower urinary tract symptoms because the damaged urothelium can trigger local afferent nerve activation and impair bladder function (14,15).

Conclusions

Fungal UTIs in paediatric age group represent a major isolate causing UTI. The distribution and frequency of isolates may show difference among centers and units. The pandemic of the covid-19 correlates with the increased prevalence of lower urinary tracts funguria cases as well as hyphae score that too in FH++++. we found significant number of cases of FH++++ in age group of 1-4 yrs which suggest future target age group in paediatric population. Yeast identification and testing in these patients is helpful in finding the optimal antifungal chemotherapy. Treatment for asymptomatic and low-risk patients with FH+, FH++ is not required. Taking in high risk consideration, conscious and careful examination by both clinician and lab technicians help these age group treated accordingly.

References

1. J. Wise et al. Genitourinary candidosis: diagnosis and treatment *J Urol* (1976)
2. C.A. Kauffman et al. *Torulopsis glabrata* renal infection *Am J Med* (1974)
3. P.B. Irby et al. Fungal bezoars of the upper urinary tract *J Urol* (1990)
4. R.H. Rubin. Infectious disease complications of renal transplantation *Kidney Int* (1993)
5. G.J. Wise et al. Amphotericin B as a urologic irrigant in the management of noninvasive candiduria *J Urol* (1982)
6. J.R. Graybill et al. Ketoconazole therapy for fungal urinary tract infections *J Urol* (1983)
7. B.J. Guglielmo et al. Management of candiduria *Int J Antimicrob Agents* (1994)
8. G. Kraatz. Therapie der Pilzinfektion Nieren- Hochdruckkr (1996)
9. panel S. Krcmery a, M. Dubrava a, V. Krcmery Jr. b. Fungal urinary tract infections in patients at risk *International Journal of Antimicrobial Agents* Volume 11, Issues 3–4, May 1999, Pages 289-291
10. Can O, Erkoç M, Ozer M, Karakanli MU, Otuncemur A. The effect of COVID-19 on lower urinary tract symptoms in elderly men. *International Journal of Clinical Practice*. 2021;75
11. Mumm JN, Osterman A, Ruzicka M, Stihl C, Vilsmaier T, Munker D, et al. Urinary frequency as a possibly overlooked symptom in COVID-19 patients: does SARS-CoV-2 cause viral cystitis? *Eur Urol*. 2020;78.4:624–628.
12. Grover S, Srivastava A, Lee R, Tewari AK, Te AE. Role of inflammation in bladder function and interstitial cystitis. *Therapeutic Advances in Urology*. 2011;3:19–33.
13. Fry CH, Vahabi B. The Role of the Mucosa in Normal and Abnormal Bladder Function. *Basic & Clinical Pharmacology & Toxicology*. 2016;119(Suppl 3):57–62.