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Original Research Article

Clinical profile of mucormycosis in paediatric patients in tertiary care centre in North West Rajasthan

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Abstract

Objectives: This survey aims to find out the possible risk factors including those during developmental period of the child that may contribute to the increased susceptibility of acquiring mucormycosis in paediatric age group.
Methods: A cross sectional observational study was done over a period of 3 months in a tertiary care centre involving all the paediatric patients with confirmed diagnosis of mucormycosis.
Results: 12 patients in paediatric age group with mucormycosis were included in this study. 66.6% patients belonged to rural areas. 33.3% children were born preterm. 2 of them had haematological malignancies. Neutrophil to lymphocyte ratio was raised in 59% patients.
Conclusion: Many etiological factors exist which contribute to the increased susceptibility of mucormycosis in children. They need to be explored. This study will contribute in better understanding of the factors responsible for causing mucormycosis in paediatric population. This will ultimately enhance the management and prognosis of the disease.
Keywords: Mucormycosis, paediatric, risk factors.

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1. Introduction

In the midst of the second wave of covid -19 infections, the nation has witnessed an enormous rise in cases of rhino orbital cerebral mucormycosis. It commonly affects immunocompromised people, especially those with uncontrolled diabetes[1]. Although a few cases have been reported in immunocompetent hosts as well[2]. Time and again, many cases of mucormycosis have been reported in paediatric age group as well[3],[4].

Mucormycosis/Zygomycosis is a fungal infection that can be highly invasive and caused by an opportunistic fungi that belongs to the class Phygomycetes and order Mucorales[5]. It is the third most common invasive fungal infection in the children, after *candida* and *aspergillus* species[6]. This fungi can invade the nose, sinus, orbit, central nervous system, lungs, gastrointestinal tract, jaw bones, skin, heart and kidneys[7]. Prematurity is an established risk factor responsible for invasive mucormycosis[8].

COVID-19 virus creates a hypoxic environment with high levels of glucose and ferritin, and attenuated phagocytic activity of leukocytes due to immunosuppression by the virus itself and the corticosteroids used in its treatment[7]. This further creates a highly conducive environment for the fungal spores to germinate[7]. The innate immune system of our body, mainly the neutrophils and macrophages play an important role in preventing the invasion of the fungi in the body[9].

Diagnosis of mucormycosis in children in initial stages requires a high level of suspicion and knowledge by the clinician. Hence, this survey aims to identify the possible contributing factors for development of rhino orbital cerebral mucormycosis in the paediatric age group.

2. Materials and Methods

This was a cross sectional observational study carried out at a tertiary care centre. Sample size of this study was 12. All the patients with histopathologically confirmed diagnosis of mucrmycosis who were admitted in the mucormycosis ward of the hospital were included. Data

was collected from patients who were admitted between 1st April 2021 to 30th June 2021. The age group was 1 to 18 years. Informed consent was obtained by the informants. A questionnaire [Appendix 1] was filled which consisted of the demographic details of the patient, socio economic status, presenting complaints, history of covid infection in the past, antenatal history, natal history and postnatal history of the mother, feeding history, immunization history of the child, age at which various developmental milestones were achieved by the child. Various investigations were ordered which included blood investigations like complete blood count including neutrophil: lymphocyte ratio, C - reactive protein and D-Dimer levels, fasting blood sugar values, bleeding time and clotting time. Also, MRI of brain, orbit and paranasal sinus were done and analysed by appropriate statistical methods.

APPENDIX 1

Sr. No.	Quaternaries	Response
1.	Informant	
2.	Name of patient	
3.	Age	
4.	Gender (Mark only one oval)	Male
		Female
		Other
5.	Residential area (Mark only one oval)	Rural
		Urban
6.	Socio economic status	
7.	Presenting complaints (Mark only one oval)	Ocular complaints
		Non ocular complaints
		Both
8.	Covid history (Mark only one oval)	Positive
		Negative
		Antenatal history
9.	Duration of pregnancy (Mark only one oval)	Full term
		Pre term
10.	Illness during pregnancy (Mark only one oval)	DM
		HTN
		Pre eclampsia
		Antepartum haemorrhage
		Other
11.	Infection during pregnancy (Mark only one oval)	Rubella
		UTI
		Syphilis
		TB
		Other
12.	Drugs taken during pregnancy (Mark only one oval)	Iron
		Multivitamins
		Other
13.	X Ray exposure in first trimester (Mark only one oval)	YES
		No
14.	Tetanus toxoid 2 doses (Mark only one oval)	Yes
		No
15.	**Natal history**	
16.	Place of delivery (Mark only one oval)	Hospital
		Home
17.	Delivery conducted by (Mark only one oval)	DAI
		Trained heath worker
18.	Labour time (Mark only one oval)	Normal
		Prolonged
19.	Type of delivery (Mark only one oval)	Cesarean
		NVD
20.	Any complication during delivery E.g. Abnormal bleeding (Mark only one oval)	Yes
		No
		Other
21.	Postnatal history	
22.	After birth (Mark only one oval)	Cried immediately
		Cyanosed
		Apneic
23.	Need of resuscitation (Mark only one oval)	Yes
		No
24.	Birth weight	
25.	Feeding history	
26.	Onset of feeding (Mark only one oval)	Within half an hour of birth
		More than half an hour of birth
27.	Type of feed (Mark only one oval)	Breastfeed
		Bottle feed
28.	Immunization history	
29.	Immunized for (Mark only one oval)	DPT
		MMR

		HEPB
30.	Developmental Milestones	Neck holding
		Standing
		Walking
		Bowel and bladder control
31.	Past history- (Mark only one oval)	History of diarrhoea
		History of jaundice
		History of respiratory infection
32.	Allergic to any drug (Mark only one oval)	Yes
		No
33.	Any regular medication	
34.	Family history	
35.	Consanguineous marriage (Mark only one oval)	Yes
		No
36.	Similar illness in siblings (Mark only one oval)	**Yes**
		No
	Investigations	
37.	Haemoglobin	
38.	Platelet (Mark only one oval)	1.5 Lac- 4 Lac
		More than normal
		Less than normal
39.	WBC (Mark only one oval)	4500 To 11000
		More than normal
		Less than normal
40.	Neutrophils (Mark only one oval)	40% TO 60%
		Less than normal
		More than normal
41.	Lymphocytes (Mark only one oval)	18% TO 45%
		More than normal
		Less than normal
42.	Neutrophil: Lymphocyte ratio (Mark only one oval)	1 to 3
		Less than 1
		More than 3
43.	CRP (Mark only one oval)	Less than 3mg/dl
		more than 3mg/dl
44.	D Dimer (Mark only one oval)	Less than 0.5
		More than 0.5
45.	FBS (Mark only one oval)	70-100 mg/dl
		Less than normal
		More than normal
46.	Bleeding time (Mark only one oval)	1 to 8 min
		Less than normal
		More than normal
47.	Clotting time (Mark only one oval)	8-15 min
		Less than normal
		More than normal
48.	MRI brain (Mark only one oval)	Normal
		Abnormal finding
		Other
49.	MRI Orbit (Mark only one oval)	Normal
		Abnormal
		Other
50.	MRI PNS (Mark only one oval)	Normal
		Abnormal
		Other
51.	Recent surgical history (Mark only one oval)	No
		Yes
		Other
	Vitals	
52.	PR (Mark only one oval)	Normal for age
		More
		Less
		Other
53.	RR (Mark only one oval)	Normal for Age
		Less
		More
		Other
54.	SPO2 (Mark only one oval)	>= 95%
		Less than 95%
55.	BP (Mark only one oval)	Normal for age
		More
		Less
		Other

2.1 Statistical methods

Percentages were calculated from the data that was obtained by the patients and was analysed to draw the inferences.

3. Results and discussion

Out of 12 patients who were included in this survey, 83.3% were males and the rest 16.7% were females. 66.6% patients belonged to rural areas and the remaining 33.4% belonged to urban areas (Figure 1). All of them were categorised into low socio economic status according to the Kuppuswamy scale. 58.3% of patients presented to the hospital with both ocular and systemic complaints whereas 16.6% patients presented with only ocular complaints and 33.3% patients showed to the hospital with only systemic complaints. Only 25% were tested positive for Covid-19 infection through RT-PCR in the past.

The mother or guardians of the child were enquired thoroughly about the antenatal, natal and postnatal history. In antenatal period, 33.3% children were born preterm (Figure 2), only 2 mothers were diagnosed with gestational diabetes mellitus, all the mothers were compliant with multivitamin and iron supplement intake. 75% mothers got tetanus toxoid shots at anganwadi centres in their locality during pregnancy. In natal history, 41.6% children were born in hospitals by trained health care workers. The remaining 58.4% deliveries were conducted at home through dais. 83.3% deliveries were normal vaginal deliveries and 16.7% deliveries were cesarean. Fortunately, all the deliveries were uneventful. In postnatal history, all the 12 children cried immediately after birth. There was not any history of apnoea and cyanosis in the children just after birth. 66.6% of patients were fully immunized according to the National Immunization Schedule. As per the informants, all the developmental milestones such as neck holding, standing, walking and bowel and bladder control were attained by all the children included in this study at an appropriate time. Interestingly, 2 children were reported to be taking chemotherapy for leukemias namely acute lymphocytic leukemia and B cell lymphoblastic leukemia.

In blood investigations, the neutrophil counts were raised in 63.6% patients and were within normal range in the rest 36.4% patients. The lymphocyte counts were decreased in 54.5% patients and were within the normal range in the remaining patients. Thus, the neutrophil to lymphocyte ratio values were increased to more than 3 in 59% of patients (Figure 3). C- reactive protein levels were surprisingly normal in range (<3mg/dl) in 83.3% patients and D-dimer levels were within normal range (< 0.5) in 55% of patients. Fasting blood glucose levels were within normal limits of 70-110 mg/dl in 87.5% of patients. Magnetic resonance Imaging was being done for brain, bilateral orbits and paranasal sinus. MRI brain scans were reported to be normal for all the 12 children. MRI bilateral orbit were abnormal in 90.9% patients whose reports showed orbital cellulitis, proptosis of eye ball, fat stranding and edema in the periorbital region and bulky extraocular muscles. In 95.5% patients, MRI of paranasal sinus showed findings such as mucosal thickening and altered signal intensities in maxillary sinus, sphenoid sinus, ethmoid sinus and frontal sinus.

Figure 1: Population

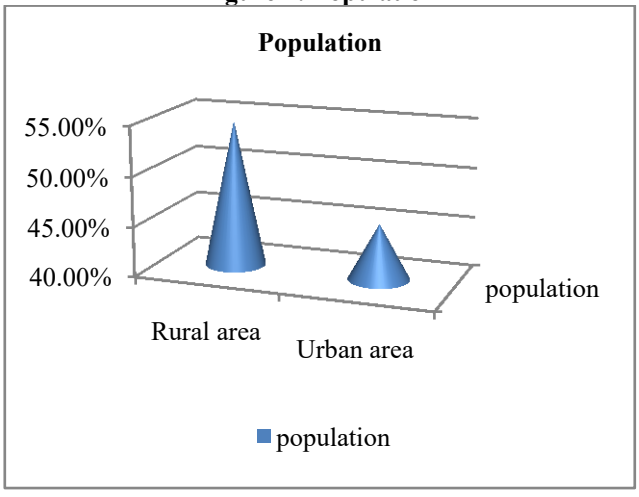


Figure 2: Gestation Period

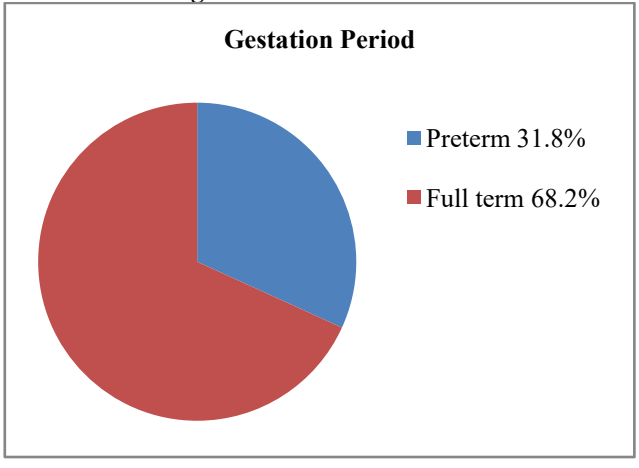
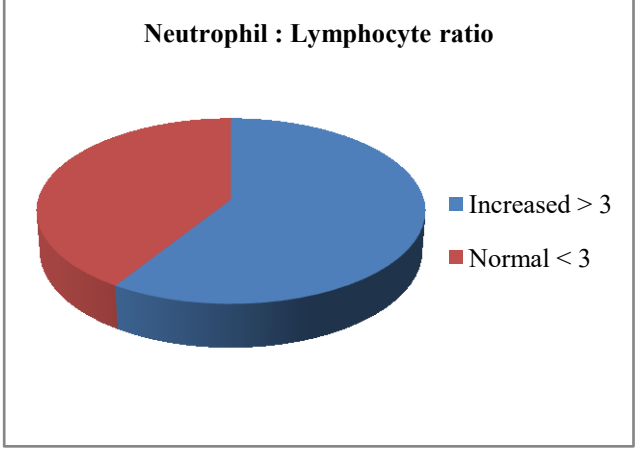


Figure 3: Neutrophil: Lymphocyte ratio



4. Discussion

Majority of the patients were residents of rural areas which indicated that mucormycosis is more common in people in rural areas. The possible reason could be frequent contact of rural population with soil and poor hygeinic practices.

The presenting ocular complaints by the children included pain in the eyes, redness in the eyes, ptosis, lid swelling, and outward protrusion of the eyeball, chemosis of conjunctiva and diminution of vision. The systemic complaints included fever, headache, nasal discharge and facial pain. Not all of the patients had COVID-19 viral infection in the past which suggested the possible role of other immune disregulatory mechanisms in the development of mucormycosis in paediatric age group. This prompted the researcher to enquire in detail about all the aspects of development of child including the antenatal, natal and postnatal period factors that may have played a role in increasing the susceptibility towards development of mucormycosis. This study showed that 5 children had hematological malignancies. A study by Prakash *et al* also describes that hematological malignancies are a proven risk factor for mucormycosis[10]. The neutrophil to lymphocyte ratio was also increased in more than half of the patients. It's elevated levels indicate a poor prognosis. Similar results have been reported earlier in the literature[11]. MRI of brain, orbit and paranasal sinus has been an important investigation to know the extent of the disease which further helps in planning its management.

Many researches on involvement of various organs by mucormycosis have been done earlier[1]. Since mucormycosis was being diagnosed and treated in our country earlier also, but the onset of second wave of covid 19 was found to be associated with a sudden surge in cases of rhino orbital cerebral mucormycosis in all the age groups including the children. Since mucormycosis more commonly affects the immunocompromised individuals, its occurrence in children has prompted the researchers to look into the possible contributing factors of the disease which lower the immunity in the children.

Recall bias and a small sample size are the limitations of this study. Small sample size is due to less number of cases of mucormycosis in paediatric age group. There are not many studies in our country that tell about the possible factors causing mucormycosis in paediatric patients. More research work needs to be done in this area. This might further help in prevention of invasion of this deadly fungal organism into the immune system of the children, early diagnosis and appropriate treatment of mucormycosis in children.

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References

[1]. Chakrabarti A, Singh R. Mucormycosis in India: unique features. *Mycoses.* 2014; 57:85-90.

[2]. Sagar S, Kumar S, Gupta A, Singhal M, Mishra B. Successful management of a case of primary cutaneous mucormycosis in an immunocompetent host. *Wounds Compend Clin Res Pract*. 2013; 25(5):136–40.

[3]. McCrory MC, Moore BA, Nakagawa TA, Givner LB, Jason DR, Palavecino EL, *et al*. Disseminated mucormycosis in an adolescent with newly diagnosed diabetes mellitus. *Pediatr Infect Dis J.* 2014; 33(10):1094–6.

[4]. Zaoutis TE, Roilides E, Chiou CC, Buchanan WL, Knudsen TA, Sarkisova TA, *et al*. Zygomycosis in Children: A Systematic Review and Analysis of Reported Cases. *Pediatr Infect Dis J.* 2007; 26(8):723–7.

[5]. Waizel-Haiat S, Guerrero-Paz JA, Sanchez-Hurtado L, Calleja-Alarcon S, Romero-Gutierrez L. A Case of Fatal Rhino-Orbital Mucormycosis Associated With New Onset Diabetic Ketoacidosis and COVID-19. *Cureus*. 13(2): e13163.

[6]. Francis JR, Villanueva P, Bryant P, Blyth CC. Mucormycosis in Children: Review and Recommendations for Management. *J Pediatr Infect Dis Soc.* 2018; 7(2):159–64.

[7]. Sen M, Honavar SG, Bansal R, Sengupta S, Rao R, Kim U, *et al*. Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India - Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. *Indian J Ophthalmol.* 2021; 69(7):1670–92.

[8]. Pana ZD, Seidel D, Skiada A, Groll AH, Petrikkos G, Cornely OA, Roilides E. Invasive mucormycosis in children: an epidemiologic study in European and non-European countries based on two registries. *BMC infectious diseases* 2016; 16(1):1-9.

[9]. Gupta A, Sharma A, Chakrabarti A. The emergence of post-COVID-19 mucormycosis in India: Can we prevent it? *Indian J Ophthalmol.* 2021; 69(7): 1645–7.

[10]. Prakash H, Chakrabarti A. Global Epidemiology of Mucormycosis. *J Fungi.* 2019; 5(1):26.

[11]. Nalbant A, Kaya T, Varim C, Yaylaci S, Tamer A, Cinemre H. Can the neutrophil/lymphocyte ratio (NLR) have a role in the diagnosis of corona virus 2019 disease (COVID-19)? *Rev Assoc Médica Bras.* 2020; 66:746–51.