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Original Article

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To Study the Clinical Profile and Peak Expiratory Flow Rate in Bronchial Asthma in Children Aged 6 to 12 Years

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Abstract

Asthma is one of the most common chronic diseases world-wide imposing a substantial social burden on both children and adults alike. Worldwide childhood asthma appears to be increasing in prevalence, despite considerable improvement in management of the disease . In India prevalence of asthma has been found to be around 6% in majority of survey, but it has been reported to vary from 2-17% in different study population, affecting on average about 3-11% of adults, 3-5% of paediatric population. The symptoms of the disease can start at any age, but in majority it starts before 10 years of age. *Aims and Objectives:* To study the clinical features of bronchial asthma and the peak expiratory flow rate(PEFR)in patients with acute exacerbation of bronchial asthma and to assess objective response of PEFR to bronchodilator therapy in group of 40 children visiting the department of pediatrics in a city hospital. *Material and Methods:* Data was collected by using pre-tested proforma meeting the objectives of the study. The purpose and technique of the study was carefully explained to the subjects and informed consent was taken.Age and sex matched control group of 100 was taken from the same population as the lung function tests are affected by certain variables like age, sex, stature and environmental conditions Detailed clinical history, thorough clinical examination was taken. Relevant investigations were done. Instrument used to measure PEFR was "The miniature Wright's peak flow meter". *Results***:** There was significant reduction in PEFR in all the age groups of the study group as compared to the control group which was easily measured using the miniature Wright's peak flow meter in both outdoor and admitted patients.

Keywords: Asthma; Children; Peak Expiratory Flow.

Introduction

Asthma is a syndrome characterized by chronic airway inflammation and increased airway hyper-responsiveness leading to symptoms of wheeze, cough, chest tightness and dyspnoea. It is characterized functionally by the presence of airflow obstruction which is variable over short periods of time, or is reversible with treatment. There are several inflammatory mediators that contribute the characteristic patho-physiological changes that lead to symptoms of asthma.

Asthma is one of the most common chronic diseases world-wide imposing a substantial social burden on both children and adults alike. Asthma occurs in all countries regardless of the level of development but varies greatly between populations, even within countries. There is evidence that over the last 20 years its prevalence has considerably increased, especially among children.

The prevalence of asthma symptoms in children has been described as ranging from from 0 to 30 percent in different study populations. Worldwide childhood asthma appears to be increasing in prevalence, despite considerable improvement in management of the disease [2]. In India prevalence of asthma has been found to be around 6% in majority

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of survey, but it has been reported to vary from 2-17% in different study population, affecting on average about 3-11% of adults, 3-5% of paediatric population [3].

The symptoms of the disease can start at any age, but in majority it starts before 10 years of age. Although many patients have mild disease, any person with asthma can develop a severe exacerbation [4] The childhood asthma is responsible for significant proportion of school days lost. A wide range of different methods to assess the level of airflow limitation exists. But two methods have found wide spread acceptance in patients over 5 years of age. These are the measurement of forced expiratory volume in 1 sec (FEV1) and its accompanying forced vital capacity and the measurement of peak expiratory flow [5].

Aims and Objectives

1. To study the clinical features of bronchial asthma in children visiting the department of pediatrics, in a city hospital .
2. To study the peak expiratory flow rate(PEFR)in patients with acute exacerbation of bronchial asthma and to assess objective response of PEFR to bronchodilator therapy.

Material and Methods

A group of 40 children with symptomatic bronchial asthma attending the Department of pediatrics, Government Hospital, Gandhi Nagar, Jammu.

Inclusion Criteria

The children between age group of 6 to 12 years with exacerbation of asthma.

Exclusion Criteria

The children with following conditions were excluded from the study

- The children with abnormal chest radiography and patient with history of heart failure.
- Children with life threatening asthma as defined by British guidelines on management of asthma.
- The patient with history of any systemic disease which is known to involve respiratory system.
- History of surgery involving cardiovascular or respiratory system.
- And finally the children with history of contact with patients of tuberculosis or past history of having been treated for the same disease;

Collection of Data

Data was collected by using pre-tested proforma meeting the objectives of the study. The purpose and technique of the study was carefully explained to the subjects and informed consent was taken. Detailed clinical history, thorough clinical examination was taken. Relevant investigations were done. Instrument used to measure PEFR was "The miniature Wright's peak flow meter". Control group was selected from children attending OPD of hospital for minor ailments and without any systemic diseases. Their height, weight and age; detailed history, clinical examination and PEFR findings were recorded in details .

Techniques of Performing PEFR

The patients were selected according to the criteria laid down earlier. The purpose and technique of the study was carefully explained to the subjects and informed consent was taken from the parents . PEFR was measured before giving nebulization with salbutamol. Post bronchodilator PEFR was recorded 10 min after nebulization with 0.5% solution of salbutamol. The patients were advised to take maximum inspiration and then to exhale forcibly into the flow meter with nose closed after satisfactory trial blows and then recordings were taken. Care was also taken to maintain airtight seal between lips and mouth piece of the instrument. For analysis the maximum of 3 recordings were taken.

Results

The 40 children in the age group between 8 -12 years with symptomatic bronchial asthma visiting OPD or admitted to hospital were randomly selected for the study. Age and sex matched control group of 100 was taken from the same population as the lung function tests are affected by certain variables like age, sex, stature and environmental conditions. Age wise distribution of children was as follows-there were 11 children (6 boys and 5 girls)in age group of 8-9 years, 7 (4 boys and 3girls) patients in age group 9-10 years,11children (8 boys and 3 girls) in the age group 10-11 years and 11 children in age group 11-12 years (5 males and 6 females)

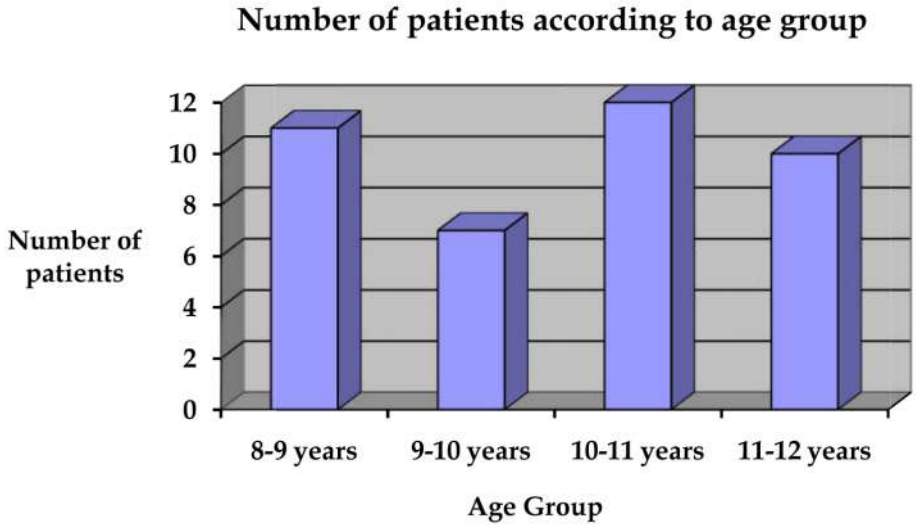
Family history of asthma was present in 21 cases. History of food allergy was present in 16 cases.

Absolute Eosinophilic count (AEC) was >400/mm3 in 17 cases. Abnormal Chest X ray (hyperinflated lung fields) was found in 24 cases.

In this study as per the history given by attendants, the cold air was the most frequent precipitating factor in 17 cases followed by URTI in 15 cases, dust in 5 cases and cold food in 5 cases and no precipitating cause could be found in the remaining 8 cases.

In the study group cough and wheeze was present in all cases (100%), chest retraction in 25 cases, fever in 15 cases, nocturnal cough was present in 12 cases. The mean respiratory rate was significantly higher in study group as compared to control group .

Fig. 1:



There was significant reduction in PEFR in all the age groups of the study group as compared to the control group.

Discussion

40 children with symptomatic bronchial asthma, between age group of 8 and 12 years were selected by using simple random sampling technique and peak expiratory flow rate was measured before and after bronchodilator therapy with the help of mini Wright peak flow meter.

The study group was divided into 4 groups based on age. Age and sex matched control group with normal health status was taken from the same population visiting the hospital for unrelated condition . It is known that peak expiratory flow rate varies with age, sex, height and weight. Therefore important consideration in study of PEFR was to ensure matching of these variables between study group and control group.

Results in this study show that in the both groups (study group and control group), sex, height, weight and age were nearly equally distributed among cases and controls with nearly equal mean SD. Since cases and controls were sampled from the same population, they have same socioeconomic background. Thus this ensures adequate matching for comparability between cases and controls.

In present sex -wise distribution of cases in all four groups revealed slightly male predominance in all groups as there were 6 boys and 5 girls in age group of 8-9 years, 4 boys and 3girls in age group 9-10 years, 8 boys and 3 girls in 10-11 years and 5 males and 5 females in the age group of 11-12 years . Several studies have shown that asthma is more common and more severe in boys than in girls [6-9].

In present study 40 (80%) children were from urban area and 10 (20%) children were from rural area. This shows that in our study there is urban predominance. This is in concordance with study by Aligne et al [10], which found out that children in urban area are at increased risk for asthma. The high incidence of asthma in urban populations compared with a significantly lower incidence in rural populations suggests that environmental risk factors have key role [11]. Chakvarthy et el [12] studied prevalence of asthma in urban and rural children in Tamil Nadu and found that 22% of urban and 9% of rural children (6-12 yrs of age) reported breathing difficulty and concluded that the prevalence of asthma, breathing difficulty and nocturnal cough was significantly higher among urban children. In another study, authors found that asthma prevalence was more among urban children (1m6.6%) as compared to rural (5.7%) children [13].

The clinical course of asthma encompasses acute exacerbation of cough, wheeze and chest retraction. In this study, all children had cough and wheeze (100%) as the predominant symptoms on presentation in hospital and chest retraction was seen in 22 children (44%) on clinical examination. This shows that during the attack, there is increased work of breathing and respiratory rate increases to maintain normal pa02 and Pco2 in blood (P < .000).

In present study, cold air was the most frequent precipitating factors for asthma constituting 48%, followed by URI (30%), dust (16%) and cold food (06%). Ratageri et al [14] studied precipitating factors for mild and severe asthma. They identified cold air in 61.7%, URI in 50%, smoke in 30%, dust in 46.6%, cold food in 63.3% of cases as precipitating factors associated with mild asthma and cold air in 83.3%, URI in 70%, smoke in 56.6%, dust in 46.6%, cold food in 8.3% as precipitating factor in children with severe asthma. Tomac et al [15] studied prevalence and risk factors for childhood asthma and concluded that family history of allergy, symptoms or diagnosis of allergic rhinitis and bronchitis and male gender were found to be significant predictors for asthma symptoms .

Asthma is an atopic disease, some studies [16] have showed strong genetic component in atopic disease including asthma. In this study, family history of Asthma was present in 20 (40%) children. In a study involving genetic and environmental factors associated with asthma in school children it was reported that , the family history of asthma contributed more to childhood asthma than indoor and outdoor environmental factors [16]. Blair et al [17] found that 73% of those asthmatics having a first-degree relative with an atopic condition , had chronic recurrent asthma at follow up. In this study we found that grandparents were the predominant category affected among family members and food allergy was found

Table 1:

Peak expiratory flow (pre-bronchodialator)	Peak expiratory flow(post bronchodilator)	P-value
207.22 ± 37.65	237.87 ± 36.80	0.001 (H.S.)

Table 2: Showing Mean Pefr in Four Age Groups

Peak expiratory flow(post bronchodilator)in patients	Controls(Healthy children)	P-value
237.87±36.80	258.60±36.82	0.001 (H.S.)

Table 3:

Age group(years)	Pre-bronchodilator	Post-bronchodilator	Control
8-9	169.18	200	212.36
9-10	201.42	233.28	255.57
10-11	239	268.75	285.75
11-12	215	245.20	279

in 2 (4%) cases. PenerdMornad C [18] et al studied prevalence of food allergy and its relationship to asthma and allergic rhinitis in school children and found that about 2.1% of children reported symptoms of food allergy Since Asthma is an atopic disease, it is usually associated with an increase in eosinophil count. The PEFR was studied in 4 groups based on age. The mean PEFR with SD before giving bronchodilator was 207.22 ±37.65 1/min and after bronchodilator was 237.87±36.80 1/min in our study. Applying paired 't' test. the mean value of PEFR before and after bronchodilator therapy in study group was highly significant (P < 0.001). The mean PEFR in study group was then compared with mean PEFR in control group in all 4 groups. There was significant reduction in PEFR (l/min) in study group (237.87±36.80)as compared with control group (258.60±36.82). The percentage of improvement was again statistically significant (P<0.001) after bronchodilator therapy. Statistical analysis shows significant reduction of PEFR in asthmatic patients. Thus to summerise , there was significant reduction in PEFR (l/min) in study group as compared with control group across all age groups .

Conclusion

Thus in a study involving 40 children with symptomatic bronchial asthma, between age group

Table 4: Showing the basic data of cases and controls who participated in the study

S. No.	Age	Sex	Height (centimetres)	Peak expiratory flow (pre-bronchodialtor)	Peak expiratory flow(post-bronchodilator)	PEP in controls(of same age and sex)
1.	8 years	Male	122	130	165	172
2.	8 years 3 months	Male	131	150	195	212
3.	8 years 6 months	Female	128	135	180	192
4.	8 years 6 months	Female	129	142	190	192
5.	8 years 9 months	Female	132	170	210	212
6.	8 years 9 months	Female	130	176	195	212
7.	8 years 9 months	Male	134	190	235	212
8.	8 years 9 months	Male	136	186	220	233
9.	8 years 9 months	Male	139	200	240	233
10.	9 years	Female	135	182	232	233
11.	9 years	Male	139	200	142	233
12.	9 years 3 months	Male	138	190	240	233
13.	9 years 3 months	Male	142	210	245	266
14.	9 years 6 months	Male	140	190	235	266
15	9 years 6 months	Female	136	180	220	233
16.	9 years 6 months	Female	138	180	195	233
17.	9 years 9 months	Male	146	220	246	279
18.	9 years 9 months	Female	141	240	252	279
19.	10 years 3 months	Male	140	214	252	266
20.	10 years 3 months	Male	139	190	242	266
21.	10 years 6 months	Male	145	240	262	279
22.	10 years 6 months	Female	142	240	256	266
23.	10 years 9 months	Female	144	220	240	279
24.	10 years 9 months	Male	146	190	240	279
25.	10 years 9 months	Male	149	260	294	303
26.	10 years 9 months	Male	150	272	286	303
27.	10 years 9 months	Female	149	238	260	303
28	10 years 9 months	Male	152	280	310	303
29.	10 years 9 months	Male	150	272	305	303
30.	11 years	Male	148	252	278	279
31.	11 years 3 months	Female	142	240	252	266
32.	11 years 3 months	Female	139	200	212	233
33.	11 years 6 months	Male	146	210	238	279
34.	11 years 6 months	Male	149	216	246	303
35.	11 years 6 months	Male	150	270	292	329
36.	11 years 6 months	Female	142	190	230	266
37.	11 years 9 months	Female	139	180	210	266
38.	11 years 9 months	Female	140	194	238	266
39.	12 years	Male	149	230	284	303
40.	12 years	Female	146	220	250	279

of 8 and 12 years ,the peak expiratory flow rate was measured before and after bronchodilator therapy with the help of mini Wright peak flow meter. There was significant reduction in PEFR (l/min) in study group as compared with control group across all age groups, and he percentage of improvement was again statistically significant (P<0.001) after bronchodilator therapy.

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Original Article

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Assessment of the Myocardial Velocity by Tissue Doppler Imaging in Children of Sickle Cell Anemia

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Abstract

Background: Sickle cell anemia (SCA) is a formidable problem in India, and is more prevalent in Maharashtra. Cardiovascular events and complications are the leading cause of mortality and morbidity in patients with SCA. The aim of this study was to determine the issue Doppler Imaging (TDI) changes in left ventricular function in children suffering from SCA. *Methods and Results:* This case controlled study comprised of 20 cases of SCA, and 20 non-anaemic controls with normal haemoglobin and electrophoresis pattern. M-mode, Two-Dimensional, Doppler and Tissue Doppler Imaging (TDI) measurements of patients and controls were performed. In the study cases, age ranged from 5 years to 15 years with the mean age of 9.91 years. There were 12 males and 8 females in the study cases. Patients with SCA had significantly larger left atrial, and left ventricular dimensions. The ejection fraction and shortening fraction were lower in the cases, but the difference was not statistically significant. The LV tissue Doppler of the lateral annulus of mitral valve in SCD compared with control showed higher E′/A′ ratio and reduced S wave which was statistically insignificant ($p > 0.05$), similar finding were present at the level of interventricular septum and lateral annulus of tricuspid valve. *Conclusions*: TDI is a useful non-invasive technique to study the changes in cardiac structure and function. SCA in children results in a volume-overloaded heart with a significant increase in left ventricular dimensions.

Keywords: Sickle Cell Anemia; Tissue Doppler Imaging; Ventricular Function.

Introduction

Sickle cell anemia was first described in a west Indian student by Herrick in 1910. It is a significant health problem in India mainly in the central part of Maharashtra. The prevalence of SCA in different communities of Maharashtra ranges from 1.9% to 33.5%. Most of the SCA patient's has abnormal cardiac finding which are primarily the result of chronic anemia and the compensatory increased cardiac output. The disease is characterized by complications such as anemia, pulmonary hypertension, lungs, kidneys, spleen, and brain injuries due to deprived tissues and organs from oxygen-rich blood. The cardiac function in SCA is best evaluated by using echocardiographic modalities as two-dimensional, M-mode, Doppler, and TDI [1-4]. Doppler echocardiography is widely used to assess noninvasively the mitral and tricuspid flow for the assessment of diastolic function. TDI is a Doppler ultrasound modality that records regional systolic and diastolic velocities within the myocardium and time to peak myocardial velocities with high temporal resolution. It allows quantitative measurement of both systolic and diastolic velocities directly from the ventricular myocardium with the determination of the extent of mitral annular displacement in systole and diastole. It can be used at any point of the ventricular myocardium to give information on the regional wall motion. It can also be drawn upon in the assessment of ventricular

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dyssynchrony in biventricular pacing. The measurement of both systolic and diastolic components can be made simultaneously with Myocardial performance index (MPI) or Tei index [5-7]. It is used for the evaluation of the systolic and diastolic functions of the ventricle and is correlated with the index of the cardiac function in cardiac catheterization and magnetic resonance-derived right ventricular ejection fraction [8-9]. The assessment of peak systolic velocities of the ventricular myocardium with TDI is of incremental value to conventional echocardiography to assess global and regional ventricular performance in various clinical conditions [10]. TDI and transthoracic echocardiography are two useful tools to assess the risk of SCD. The present study was conducted to evaluate the cardiac functions and structure using TDI among children suffering from SCA compare to normal samples.

Material and Methods

This study was carried out in the Department of Pediatric, AVBRH hospital, Sawangi (Meghe), Wardha. It was a hospital based case-controlled study conducted from January 2015 to May 2017. The study comprised of 20 cases of sickle cell anemia (Hb SS), and 20 non-anaemic controls with normal haemoglobin and electrophoresis pattern. The control group was comparable in age and sex, free from cardiovascular disorder and not taking any cardioactive drugs. The study protocol was approved by the JNMC ethical institutional committee. Patients with SCA were excluded if they had a history of recent blood transfusion within three weeks, had hemoglobinopathy other than SCA, rheumatic heart disease, congenital heart disease, or advanced renal or hepatic failure. Detailed general and systemic examination was done in cases and controls with special emphasis were given for pulse, jugular venous pulse, blood pressure and presence of heart murmur. By using Phillip echocardiography machine, two-dimensional (2D), M-mode, Doppler and Tissue Doppler Imaging was performed.

The measurements of M-mode parasternal short-axis were conducted at end-diastole for interventricular septal thickness, LV posterior wall thickness and left ventricular diameter in diastole and systole. The fractional shortening and ejection fraction was estimated using M-mode and Simpson in the parasternal long- and short-axis views as well as in the apical four-chamber view. Also, the apical four-chamber view was used to record LV inflow velocities in which the peak flow velocities of the LV inflow in early diastole (E) and late diastole with atrial contraction (A) were measured. E/A velocity ratios were calculated for each cardiac cycle.

TDI was performed in the apical four-chamber view by placing a sample volume at three different site i) Lateral border of mitral valve annulus ii) Interventricular Septum and iii) Lateral border of tricuspid annulus. The Doppler beam was aligned as parallel as possible to the direction of the maximum annular motion. Peak systolic and diastolic velocities and timings of peak velocities at the LV and RV were assessed with TDI in all subjects. The following parameters were recorded: systolic velocity (S‘), early diastolic velocity (E‘), late diastolic velocity (A‘) and time intervals; isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT) and ejection time (ET) at each site. The isovolumic relaxation time (IVRT’) was measured from the end of the S’ wave to the onset of the E’ wave, and the isovolumic contraction time (IVCT’) was measured from the end of the A’ wave to the onset of the S’ wave. The E/E’ ratio was also calculated. Each TDI velocity or time interval was measured on 2-3 consecutive cardiac cycles and subsequently averaged. Then calculation of the mean E/E‘ (mitral inflow E wave/E‘ mitral annulus velocity) ratio was done. According to the E/E‘ ratio, patients were classified into: patients with E/E‘≥ 15 (diastolic dysfunction), patients with E/E‘≥ 8 but less than 15 (suspected diastolic dysfunction) and those with E/E‘< 8 (without diastolic dysfunction). All data were obtained according to the recommendtions of the American Society of Echocardiography. The TDI Tei index is the IVCT plus IVRT divided by the ejection time (ET) and affords a simultaneous measurement of the atrioventricular inflow and ipsilateral semilunar outflow Doppler velocities [11-12].

Statistical Analysis

Data are expressed as mean± standard deviation (SD). The independent samples t-test was used to compare echocardiographic data between patients and controls. A value of $p < 0.05$ was considered statistically significant.

Results

In the study cases, age range was from 4 years to 15 years with the mean age of 7.91 years. There were 12 males and 08 females in the study group. On cardiovascular examination, mean heart rate was

82±11 beats per minute (bpm), mean blood pressure was 96±14/68±4 mmHg. On auscultation, 2 cases revealed an ejection systolic murmur heard maximally in 3rd left intercostal space parasternally. Patients with SCD compared with the control had a significant increase in the diameter of left atrium and left ventricle. There were no significant differences observed between the two groups for the left ventricle ejection fraction percentage. The ejection fraction and shortening fraction were lower in the cases, but the difference was not statistically significant. On Doppler study, 'E' and 'A' wave amplitude was higher in SCA cases as compared to the control which was not statistically significant. Standard Echocardiography parameters between cases and controls shows in Table 1. The LV tissue Doppler of the lateral annulus of mitral valve in SCD compared with control showed higher E'/A' ratio and reduced S wave ($p > 0.05$). The interventricular septum of tissue Doppler in SCD compared with control showed higher E'/A' ratio and reduced S wave ($p > 0.05$). In RV the tissue Doppler of the lateral annulus of tricuspid valve showed shorter S wave velocity higher E'/A' ratio as compared to control ($p > 0.05$). The results of the TDI study in the SCA cases and controls are depicted in Table 2. The isovolumic relaxation time (IVRT), isovolumic contraction time (IVCT), and Tei index were equal in both groups. Two patients had trivial tricuspid regurgitation without a significant pressure gradient.

Table 1: Standard Echocardiography parameters between cases and controls

Echocardiography Parameter	Cases (Means + SD)	Controls (Means + SD)	P Value
M-Mode			
LA	21.65± 3.81	18.36± 2.13	0.002
LVIVSd	9.61± 1.81	8.17± 3.21	0.236
LVIDd	35.65± 6.74	32.12± 2.31	0.000
Shortening Fraction	27.6± 3.08	28.7± 3.02	0.892
2-Dimension			
Ejection Fraction	59.90± 2.71	61.90± 4.65	0.984
Doppler			
Mitral E (cm/s)	115± 2.71	99± 11.12	0.991
Mitral A (cm/s)	67± 2.82	60± 1.23	0.123
Mitral E/A	1.84± 0.52	1.36± 0.51	0.999

Table 2: TDI derived parameters between cases and controls

TDI Parameter	Cases (Means + SD)	Controls (Means + SD)	P Value
TDI Lateral Mitral Annulus			
LV E' (cm/s)	17.12± 5.4	20.75± 6.2	0.983
LV A' (cm/s)	7.65± 2.60	11.05± 5.2	0.986
LV S' (cm/s)	12.1± 3.1	9.12±4.1	0.931
LV E' / A'	2.28± 0.61	2.19± 0.52	0.332
LV Tei Index	0.35± 0.07	0.32± 0.10	0.856
TDI Interventricular Septum			
Septal E' (cm/s)	12.9± 3.1	14.1± 2.13	0.876
Septal A' (cm/s)	6.62± 3.2	7.1± 1.21	0.728
Septal S' (cm/s)	9.4± 3.3	9.1± 1.22	0.562
Septal E' / A'	2.11± 6.1	2.07± 5.42	0.422
Septal Tei Index	0.33± 0.09	0.32± 0.06	0.379
TDI Lateral Tricuspid Annulus			
RV E' (cm/s)	16.2± 4.11	18.1± 1.72	0.993
RV A' (cm/s)	10.1± 5.91	10.2± 1.52	0.571
RV S' (cm/s)	13.4± 4.21	14.6± 1.23	0.825
RV E' / A'	1.87± 0.66	1.84± 0.28	0.416
RV Tei Index	0.38± 0.09	0.35± 0.11	0.874

Discussion

Sickle cell disease is an inherited disorder associated with significant morbidity. The SCD patients have abnormal hemoglobin in the RBCs, called hemoglobin S or sickle hemoglobin, because of adenine-to-thymine substitution in the sixth codon in the beta globin gene, replacing glutamic acid with valine in the beta-globin chain [13-14]. In SCA, the cardiovascular system is stressed by chronic anemia, recurrent small pulmonary artery occlusion, and myocardial hemosiderosis. Wali et al [15] reported that the dilated chamber in SCA was not associated

with any abnormality in systolic or diastolic ventricular function nor with significant hypertension. However, Lester et al [16] concluded that the major echocardiographic abnormality in SCA children was enlargement of left heart chambers; our study had similar findings. Kilinc et al [17] reported that mean left atrial dimension was increased in SCA group compared with controls ($p<0.001$), which is in concordance with the present study. Kingue et al [18] reported that the amplitudes of the mitral inflow 'E' and 'A' waves were increased, and the deceleration time (DT) was longer in the sickle cell group whereas in our study, 'E' and 'A' wave amplitude were increased in SCA cases as compared to the controls although the difference was not statistically significant. There were no abnormalities in the ejection fraction or shortening fractions. These results suggest early hemodynamic changes with progressive cardiac chamber dilation that become increasingly abnormal with growth. Notomi et al [19] assessed LV performance in 45 healthy controls by measuring rotational mechanics with TDI. In their study, LV performance increased significantly with age. Myocardial growth and an age-related increase in blood pressure may lead to greater myocardial velocities during systole in order to maintain adequate cardiac output. SCA is frequently complicated by pulmonary hypertension and cardiac involvement. Ferit Akgu et al [20] found that the LV functions were preserved in SCD patients with or without pulmonary hypertension and the RV diastolic function was disturbed only in SCD patients with pulmonary hypertension. The RV abnormal diastolic pattern may be in consequence of a rise in the RV afterload, secondary to pulmonary hypertension. Myocardial micro emboli may be caused by an ischemic area and diastolic abnormalities SCD patients, and these abnormalities are progressive with age. It should also be noted that low haemoglobin level and increased heart rate may worsen the cardiac disease in these patients [21].

TDI is an effective method for the evaluation of the cardiac function and myocardial velocities through the cardiac cycle. The Tei index is a simple parameter for the evaluation of the RV and LV functions and is correlated with the invasive measurements of the cardiac systolic and diastolic functions. TDI can record systolic and diastolic velocities during the same beat. No statistically significant changes found in cases as compare to controls in E'/A' ratio and S wave at the LV tissue Doppler of the lateral annulus of mitral valve. In patients with SCD, a chronic volume overload from prolonged anemia along with or without micro vasculopathy and myopathy, which affect all patients, may explain such abnormalities in echocardiographic examinations. Our SCA cases and controls had a normal Tei index. Prolongation of the ICT and IRT occurs in prolonged and chronic pathologic conditions such as increased LV load or an intrinsic LV myocardial dysfunction. A higher than normal Tei index is indicative of a reduced LV function. High-output state, which is seen in anemia, can also lead to heart failure. Lastly, the sickling process could directly affect the heart and induce myocardial ischemia and heart failure [5,21]. Chronic LV dysfunction in such patients maybe a significant determinant of the clinical outcome in acute states such as sickling crisis. The ejection fraction was within the normal limits in SCA cases, but it was lower than that of control group. Ghaderian M et al [22] in his study showed that Ea and Aa velocity in the mitral annulus and interventricular septum had no difference between the patients and controls (p value > 0.05), and nor was there any difference between the two groups as regards the Tei index, Ea/Aa, ejection fraction, and shortening fraction ($p > 0.05$). AboHadeed HM et al [23] reported that TDI technique appears to be more sensitive than conventional echocardiography in the early detection of myocardial dysfunction in children with SCA. This provides insights into the value of early screening and the potential for preventive therapy in children to avert cardiac morbidity and mortality in adults with SCA. The limitations of the present study was the small sample size.

Conclusion

TDI is a useful non-invasive technique to study the changes in cardiac structure and function. SCA in children results in a volume-overloaded heart with a significant increase in left ventricular dimensions. The evaluation of LV systolic and diastolic function via TDI did not indicate significant differences between SCD children compared to healthy controls.

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Original Article

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Spectrum of Nutritional Status: A Cross Sectional Study

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Abstract

Background: Pediatric malnutrition is a major cause of morbidity and mortality in developing countries including India. This malnutrition can be prevented by proper dietary advice to parents along with early diagnosis and management of malnutrition. The aim of this study was to find out the present nutritional status and its comorbid abnormalities in children attending primary school in rural Kanpur. *Objective:* To assess the prevalence of underweight, stunting, wasting and comorbid abnormalities of malnutrition in 5 to 10 years age group of school going children. *Methods:* This study was across sectional study conducted in rural primary schools of Mandhana Kanpur between December 2016 to May 2017 to know the nutritional status of school age children with coexisting morbidities with the help of anthropometric measurement and clinical examination. *Results*: A total of 400 children were studied belonging to the age group 5 to 10 years including 226 (56.5%) boys and 174 (43.5%) girls. Approximately 54% boys and 50% girls have their weight and height within normal limits. Prevalence of wasting and stunting was highest in 5 to 6 years age group in both sexes. On clinical examination highest number of children were found to be clinically anemic in both sexes but more in girls followed by presence of pharyngitis. *Conclusion*: In our study we found presence of all types of nutritional deficiency starting from under nutrition to stunting, wasting and associated abnormalities like anemia and pharyngitis. Need of the hour is more steps to be taken to overcome the nutrition gap and abolish the problem of malnutrition.

Keywords: Underweight; Stunting; Wasting; Anemia.

Introduction

Pediatric age group is the period of rapid growth, and this period is highly vulnerable period as well. In pediatrics the school age is the active growing phase of childhood [1]. Multiple factors work together to affect the growth and development of children.

Health and nutritional condition in children is best assessed by anthropometric examination which includes physical measurements like body weight, height, mid arm circumference and triceps skin fold thickness. Based on the age, sex, body weight and height, certain indices such as weight for age, height-for-age and weight-for-height have been suggested [2]. Then children are classified using anthropometric measurement in three categories: 'underweight' (less than 2 SDweight-for-age), 'stunting' (less than2SD height-for-age) or 'wasting' (less than 2SD weight-for-height). Less than 2 SD away from the CDC 2000 (Centers for Disease Control and Prevention) standards [2,3,4].

"End all forms of malnutrition by 2030." That was the challenge world leaders laid down to all of us at the end of 2015 when they adopted the Sustainable Development Goals (SDGs) [1]. At least 12 of the 17 sustainable development goals contains indicators that are highly relevant for nutrition, reflecting nutrition's central role in sustainable development [5].

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The socioeconomic status of the family and social wellbeing of the community is reflected in the nutritional status of the pediatric population. The present study in rural primary school of Kanpur, Uttar-Pradesh (UP), India, was undertaken to evaluate the overall prevalence of undernutrition and, sex wise difference if any in undernutrition, and to find out any associated comorbid abnormalities of undernutrition.

Methods

This study was across sectional study conducted by department of Pediatrics Rama Medical College Mandhana Kanpur between December2016 to May 2017. Study group comprised of 400 children from age group 5 to 10 years studying in a primary school of Mandhana. To calculate the sample size with 52% prevalence of malnutrition at 95% confidence interval and relative precision of 10%, 400number of children needed to be included in the study.

Ethical approval was obtained from ethical committee, Rama Medical College Mandhana Kanpur. All parents / guardian of children who were enrolled in the study were informed and written consent in their local language obtained from them prior to inclusion into the study.

The age of the child was determined using school records.

Measurement of weight and height of each and every child was done, using standardized technique recommended by Jelliffe in metric system [6]. Weight was measured by digital weighing machine having accuracy of 100 grs, with children standing straight, having light clothes without heavy woolens and without footwear. Heightof the children was measured using stadiometer with child standing without footwear with feet parallel and head in frankfurt plane having firm contact with the head plate, both hands hanging by the sides of child, and occiput, shoulder, buttocks, and heal touching the rod. Weight for age (underweight), height for age (stunted), weight for height (wasted) were calculated for each and every child and compared with the CDC 2000 [2,3]. Those who had values between ± 2 SD of cutoff were considered normal [4].

All the children who were included in the study were clinically examined by the pediatric resident doctors for anemia, Vitamin A deficiency by the presence of corneal xerosis, Bitot's spots and conjunctivalxerosis, hair changes like depigmentation, lustureless, easily plukable and flag sign was looked for, skin changes like dry rough skin and crazy pavement or flaky paint dermatosis was searched. Teeth were examined for caries and cavities, and ENT examination was done for pharyngitis and tympanic membrane perforation. All the children were given dewormin tablets, and those who were found anemic were given iron tablets, vitamine A was offered to those children who were having manifestations of xerophthalmia. All other children who were diagnosed to be having csom, skin and dental findings were referred to appropriate departments for further management.

Results

A total of 400 children were studied belonging to the age group 5 to 10years (Table 1). Out of the 400 students, 226 (56.5%) were boys and 174 (43.5%) were girls.

Statistical Analysis

Statistical software namely SPSS 21.0 version was used for the analysis of the data and microsoft word and excel have been used to generate tables. There is significant statistical association & proportion was found between the graphs ($p<0.001$) at 0.1% level of significance with appropriate degrees of freedom.

Undernutrition, wasting, stunting was seen in variable number of children in study group. All the data was analysed using spss software and p value with chi square analysis and no significant association was observed.

We examined the study group for coexisting deficiency disorders in which anemia and xerophthalmia was found highly significant statistically. Hair changes, skin changes, and chronic suppurative otitis media was also found to be statistically significant in study group. Dental changes and pharyngitis was present in variable number of children but it was not statistically significant. In our study it was also observed that all findings were present more in girls than in boys.

Discussion

School age is the time when children undergo physical growth, and mental, emotional and social development is also significant during this period. According to (UNESCO) 6 to 11 years age is considered as primary school age. School age is the

Table 1: Table showing spectrum of nutritional status in school age children

Age group	Normal	Under weight	Wasted	Stunted
5-6 yrs				
Boys (39)	21(53.84%)	13(33.33%)	11(28.20%)	10(25.64%)
Girls (44)	23(52.27%)	14(31.81%)	13(29.54%)	11(25%)
6-7 yrs				
Boys (41)	21(51.21%)	10(24.39%)	9(21.95%)	7(17.07%)
Girls (41)	20(48.78%)	11(26.83%)	10(24.39%)	9(21.95%)
7-8 yrs				
Boys (44)	24(54.54%)	10(22.73%)	10(22.73%)	9(20.45%)
Girls (36)	19(52.78%)	9(25%)	9(25%)	7(19.44%)
8-9 yrs				
Boys (49)	24(48.98%)	11(22.45%)	10(20.41%)	9(18.37%)
Girls (29)	14(48.28%)	9(31.03%)	7(24.14%)	6(20.69%)
9-10 yrs				
Boys (53)	29(54.72%)	13(24.53%)	10(18.87%)	9(16.98%)
Girls (24)	13(54.16%)	7(29.17%)	6(25%)	4(16.67%)

Table 2: Prevalence of Nuritional Deficiency Spectrum

Nutritional Status	Boys (N=226) No.	%	Girls (N=226) No.	%	P-value
Normal	119	52.7	89	51.1	Z=0.397
95% Confidence interval of Normal Patients	**45.5 to 58.5**		**43.6 to 58.4**		p>0.69 NS
Underweight	57	25.2	50	28.1	Z=0.67
95% Confidence interval of Normal Patients	**19.4 to 30.6**		**21.3 to 34.7**		p>0.49 NS
Wasted	50	22.1	45	25.8	Z=0.93
95% Confidence interval of Normal Patients	**15.7 to 26.3**		**18.6 to 31.4**		p>0.35 NS
Stunted	44	19.5	37	21.3	Z=0.49
95% Confidence interval of Normal Patients	**13.9 to 24.1**		**14.9 to 27.1**		p>0.62 NS

	Normal	Underweight
Boys	119	57
Girls	89	50

X2 = 0.445 p > 0.504 statistically not significant

	Normal	Wasted
Boys	119	50
Girls	89	45

X2 = 0.55 p > 0.46 statistically not significant

	Normal	Stunted
Boys	119	44
Girls	89	37

X2 = 0.198 p > 0.656 statistically not significant

	Normal	Underweight+Wasted+Stunted
Boys	119	151
Girls	89	132

X2 = 0.72 p > 0.39 statistically not significant

Table 3: Prevalence of comorbid abnormalities instudy group

Age group	Anemia	Xerophthalmia	Hair Changes	Skin Changes	Teeth Changes	Csom	Pharyngitis
5-6 yrs	14 (35.90%)	4 (10.26%)	4 (10.26%)	3 (7.69%)	7 (17.95%)	10 (25.64%)	11 (28.20%)
Boys (39)	24 (54.55%)	7 (15.91%)	10	8 (18.18%)	8 (18.18%)	10 (22.73%)	11 (25%)
Girls (44)			(22.73%)				
6-7 yrs	15 (36.59%)	3 (7.31%)	4 (9.76%)	3 (7.31%)	13 (31.71%)	7 (17.07%)	8 (19.51%)
Boys (41)	20 (48.78%)	5 (12.20%)	8 (19.51%)	4 (9.76%)	7 (17.07%)	8 (19.51%)	5 (12.20%)
Girls (41)							
7-8 yrs							
Boys (44)	13 (29.55%)	0	3 (6.81%)	0	10 (22.73%)	4 (9.09%)	6 (13.64%)
Girls (36)	17 (47.22%)	5 (13.89%)	4 (11.11%)	5 (13.89%)	8 (22.22%)	4 (11.11%)	7 (19.44%)
8-9 yrs							
Boys (49)	17 (34.69%)	0	4 (8.16%)	0	7 (14.29%)	0	0
Girls (29)	15 (51.72%)	0	4 (13.79%)	2 (6.90%)	4 (13.79%)	4 (13.79%)	6 (20.69%)
9-10 yrs							
Boys (53)	20 (37.74%)	0	3 (5.66%)	0	6 (11.32%)	0	0
Girls (24)	13 (54.17%)	0	0	0	4 (16.67%)	4 (16.67%)	4 (16.67%)

Table 4: Prevalence of Nutritional Deficiency Spectrum in Boys & Girls

Nutritional Disorder	Boys (N=226) No.	%	Girls (N=226) No.	%	P-value
Anemia	79	34.9	89	51.1	Z=3.21P<0.0013
95% Confidence interval of Normal Patients	28.8 to 41.1		43.6 to 58.4		Highly significant
Xerophthalmia	7	3.09	17	9.77	Z=2.58P<0.0097
95% Confidence interval of Normal Patients	0.8 to 5.2		5.3 to 14.17		Highly significant
Hair Changes	18	7.96	26	14.94	Z=1.96 P<0.05
95% Confidence interval of Normal Patients	4.4 to 11.4		8.8 to 19.2		Significant
Skin Changes	6	2.65	19	10.9	Z=3.40P<0.001
95% Confidence interval of Normal Patients	0.06 to 4.8		5.5 to 14.5		Significant
Teeth Changes	43	19.2	31	17.8	Z=0.51p>0.61
95% Confidence interval of Normal Patients	13.9 to 24.1		11.4 to 22.6		Not significant
CSOM	21	9.29	30	17.24	Z=2.33P<0.01
95% Confidence interval of Normal Patients	5.4 to 12.8		11.4 to 22.6		Significant
Phyringitis	25	11.06	26	14.94	Z=0.90p>0.365
95% Confidence interval of Normal Patients	6.9 to 15.1		8.8 to 19.2		Not significant

period of very rapid growth and development, and this is the time for attainment of physical, mental, social and emotional changes. As our country is a growing country population consisting of this age group is approximately one fifth. So in this light present study was conducted to assess the nutritional status of primary school age children and associated morbidities.

Although there is vast difference in the prevalence of under nutrition and wasting in different regions but in almost whole of developing world children fail to grow in length/height and weight in similar age specific pattern [7]. In our study we observed that the growth of the children was very much less than the expected reference standards by CDC 2000. Similar results were observed by other workers as well from India [8,9]. In contrast to this in children of Latin America the prevalence of underweight and thinness is found below 10% [10].

Overall under nutrition observed in study group was 25.3% in boys and 28.6% in girls whereas in a study conducted by in Karnataka among 6 to 12 years age group observed the prevalence of under nutrition in boys 32.3% and in girls 28.3%this study showed more under nutrition among boys than our study while among girls prevalence of under nutrition was almost same as in our study [11]. Another study done by from Bangalore among 5-14 years old students stunting was seen in 58.2% children, whereas in a study from Allahabad found under nutrition in 7- 10 year age group to the tune of 25% [12, 13]. In contrast to our study another study from Kashmir conducted on 5-14 years old children reported under nutrition to the tune of only 11.1%. One more study from Assam conducted by in 6-8 year old children reported under nutrition in 47.4% of children [14,15] . One more study from Navinagar Mumbai reported prevalence for stunting 16.8% and underweight 42.3% [16]. Underweight 90.0% and stunting 47.5% was reported by from Chhattisgarh [17]. Similarly from Puriliya West Bengal also reported figures of underweight 33.7% and stunting 17.0% [18].

In our study the children were found less nourished than the children from Delhi by but in other hand our study group children were better nourished than school children from Punjab [19,20]. Another study conducted by department of Community Medicine of Rama Medical College Mandhana by also showed the prevalence of under nutrition to the tune of 28% which correlated well with our results of under nutrition in boys 25% and 28% in girls [21].

In our study we found that many children were having more than one ailment. Clinically anemia was detected in 37% in boys and 50% in girls in the present study, which was more than in the children of rural school children in Punjab (22.5%) [22]. Anemia was almost same in prevalence in our study as found in a study in Bareilly [23].

In our study we found presence of dental caries also in about 20 % of boys and 22% in girls. Our results were same as also reported by similar study from rural Kanpur(21), where 25.7% children were found affected by dental caries. Another study from Pokhra including students of Government primary school found dental caries in 41.5% children [24]. On the other hand one more study reported 17.4% children suffering from dental caries [25]. Similar study from Punjab reported lower prevalence of dental caries in rural school children 11.5% [26]. Another study from Tirupati showed almost same findings as our study where dental caries was seen in 20.9% school age children [27].

In our study chronic suppurative otitis media and pharyngitis was seen in variable no of children of different age groups, more of both problems were seen

in more girls than boys and range was from 10% to 22%. Another study from Bhaktapur found csom in 22.3%[28] and study from rural kanpur found csom in 21.5% children [21].

Hair changes and skin changes in the form of lusterless, de pigmented and sparsh hair was found in 5 to 22% children and both were present more in girls. Similar findings were seen in another study in Karnataka where all these findings were seen but much less in frequency [11]. Another study which was also from Karnataka, Mysore district included jenukuruba tribal children found hair changes in more than 90% children[29]. Vit A deficiency disorders also called as Xerophthalmia is a very common finding in school age children and in our study we looked for it in form of night-blindness, bitot's spot, congectivalxerosis and corneal xerosis. All these manifestations could be detected in variable number of children in our study ranging from 6 – 11%. In a study from Karnataka all these manifestations range between 2-20%[11]. Another study from collar district of Karnataka found that Vitamin A deficiency was the commonest ocular morbidity (33.8%) which manifested as bitot spots and conjunctival xerosis [30].

Study Strength and Limitations

This study may help in treating the morbidities related to nutritional status in school going children in rural area. As this study involved only school going children it may not be representative of children in general population

Funding

Nil

Competing Interests

The authors declare that they have no competing interests.

Conclusion

This study shows that in spite of all the efforts done by government of India ,we are not able to completely eradicate the under nutrition, wasting, stunting, and various associated deficiency disorders in school age children , though the frequency of these are decreasing but still prevalent and needs to be looked for further. We should educate the society more about the nutritional needs of children and proper dietary advice should be given to children and parents.

Contribution

VKT conceived the idea of study and supervised it, BT reviewed the literature and made the design of study, GA, RA and MM participated in data collection, CT statistically analyzed the data. All authors have read and finalized the manuscript.

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Original Article

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Prevalence of Obesity and Overweight among 15-45 Years Adolescents & Adults in a Rural Area in Ahmednagar: A Cross Sectional Study

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Abstract

Background: Obesity is an important modifiable risk factor for most chronic non-communicable diseases. The objective of the study was to determine the prevalence of overweight/ obesity among adults in rural areas of Ahmednagar. *Materials and Methods:* This was a cross sectional study conducted among 150 population in rural areas of Ahmednagar. 15-45 years adolscents& adultsare interviewed from the consecutive houses with the help of a pre-tested structured questionnaire. Height, weight, waist circumference and hip circumference were measured using standard anthropometric methodology. *Results:* Mean age of the study population was 30 years. Mean BMI among women was significantly higher (24.28), compared to men (23.2) with . The prevalence of overweight and obesity in the population was 24% and 40.7% respectively, as per WHO BMI guidelines for Asians. About 51% of women and 35% of men had high waist circumference. Higher proportion of women (77.7%) had high waist-hip-ratio compared to men (48.5%). *Conclusion:* The prevalence of overweight and obesity is high among adults in rural areas in Ahmednagar.

Keywords: Obesity; Overweight; Prevalence; Rural; Maharashtra.

Background

Obesity is defined as an excessively high amount of body fat or adipose tissue in relation to lean body mass. It is a type of nutritional disorder due to imbalance between energy intake and energy expenditure resulting in positive energy balance, characterized by the abnormal growth of adipose tissue resulting in an increase in the body weight to the extent of 20% or more of the standard weight. Obesity can be estimated by measuring anthropometric measures such as body mass index (BMI), waist-to-hip circumference ratios (WHR), Waist circumference or by radiological techniques. Global epidemic of overweight and obesity is rapidly becoming a major public health problem in many parts of the world. Obesity epidemic results in substantial decrease in the quality of life, life expectancy and it accounts for heavy expenditure in provision of health care. There is a progression of nutritional transition in developing countries, characterized by a reduction of prevalence of nutritional deficiency and more occurrence of overweight and obesity. As per NFHS 3 reports [1], Punjab, Kerala, and Delhi are the states with the highest level of overweight and obesity.The percentage of women who are overweight or obese (BMI ≥ 25) is highest in Punjab (30 percent), followed by Kerala (28 percent) and Delhi (26 percent). Even with lower BMI, Asians have higher visceral adiposity than Caucasian populations. For this reason, the international task force of World Health Organization (WHO) has set lower cut-off BMI values for Asians to define overweight and obesity.

Overweight and obesity is on an increase in urban as well as rural area. The problem of obesity has been particularly increasing in Maharashtra, as there is a drastic change in living standards and life style of

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people over the recent years. Objective of this study was to determine the prevalence of overweight/ obesity among adults.

Materials and Methods

Cross sectional study was conducted amongadolscents& adults. Study population included all adolscents& adults of 15-40 years. Exclusion criteria included pregnant women. 20% relative precision and anticipated prevalence of obesity as 30% and sample size is 174. One ward is randomly selected from this panchayath. Adults are interviewed from the consecutive houses with the help of a pre-tested structured questionnaire. Information about age, sex, alcohol use, fast food consumption, exercise and smoking history was collected. Height and weight, waist and hip circumference were measured using standard anthropometric methodology. Weight was measured without shoes and with light clothing. The weighing scale was regularly checked with known standard weights. A portable anthropometric rod was used for measuring height. Waist circumference (WC) is measured with subject standing with feet 25-30 cm apart. Measurement is taken midway between inferior margin of the last rib and the crest of ilium in horizontal plane to nearest 0.1cm. The hip circumference is measured around pelvis at the point of maximal protrusion of the buttocks. Both WC and hip circumference were measured to the nearest 0.1cm. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m2). WHR was calculated as WC (cm) divided by hip circumference (cm). The classification of BMI for Asian populations, according to the World Health Organization (WHO) 2000 guideline, was used in this study. International Association for the Study of Obesity and the International Obesity Task Force have suggested lower BMI cutoff values for the definitions of overweight and obesity in Asian populations. Body Mass Index (BMI): Obesity: BMI ≥25.00 kg/m2, Overweight: BMI 23.00–24.99 kg/m2, Normal BMI: 18.50–22.99 kg/m2 and Underweight: <18.50 kg/m2 [2]. For men Waist circumference ≥ 90 cm and for women ≥ 80 cm, were considered as cut off points for defining abdominal obesity. Waist Hip Ratio >0.90 in men and >0.80 in women are taken as high. The data is entered in SPSS and analyzed.

Results

Mean age of the study population was 30. For detailed analysis, age was grouped into categories 15-24 years, 25-34 years and 35-45 years. Mean BMI among women was significantly higher, compared to men (23.2). Mean waist-circumference (WC) among men was 85 cm and mean WC among women was 81cm . Mean WHR among men was 0.9 and among women mean was 0.8 . Mean waist to height ratio among men was 51.69 (95% CI 50-52).

Table 1: Prevalence of overweight and obesity

BMI Categories	Gender Male	Total Female		95%CI
Obese	16 (33%)	45 (44%)	61(40%)	35-46%
Overweight	12 (25%)	22 (23%)	34 (24%)	19-29%
Normal	18(36%	22(23%)	40(28%)	23-33%
Underweight	04(4%)	09(8%)	13(7%)	4-10%
Total	52	98	150	

Table 2: Waist Hip Ratio (WHR) and gender

Waist Hip Ratio(WHR)	Sex		Total
	Male	Female	
Normal	26 (51%)	22 (22%)	48 (32%)
High	25 (48%)	77 (77%)	102 (67%)
Total	51	99	150

Table 3: Overweight/obesity and fast food intake

Overweight/Obesity	Fast food consumption		Total
	No	Yes	
BMI<23	27	25	52
	45%	28%	35%
BMI>=23	34	64	98
	54%	71%	64%
	61	89	150

In the study population, 35% men and 0.5% women consumed alcohol. Also 41% of men and 2% of women were smokers. Only 30% of adults are involved in at least moderate physical activity.

For men waist-circumference ≥ 90 cm and for women ≥ 80 cm, were considered as high. Overall 45% adults in this area had high WC. About 51% of women and 35% of men had high WC.

Waist Hip Ratio (WHR) >0.9 in men and >0.8 in women are taken as high for Asians. In this study, 77% of women were with high WHR, compared to 48% men (Table 3).

No significant relation found between consumption of alcohol and overweight/obesity. Overall 8% of adults had grade II obesity (BMI ≥ 30). The proportion of women (12%) having BMI ≥ 30 was significantly high compared to men (1.9%) . Among adults who are found to be having normal BMI (<23), 29% had high WC than recommended for Asians (>90cm in males and > 80 cm in women).

Discussion

As per WHO BMI guidelines for Asians, overall prevalence of obesity was 40.7% among adults and prevalence of overweight was 24% as per the study population. Among those who are obese, 8.7% had grade II obesity.

Prevalence of obesity was found to be 44.7% among women and 33 % among men in our study. Obesity was found to be more among females (33%) than males (17%) in the study by Sugathan et al. [3], in Kerala. Prevalence of obesity was higher in females in a cross-sectional survey which was carried out on adults aged 25–60 years in Delhi, India [4,5]. In a study conducted by Venkatramana *et al* [6], overall prevalence of obesity found was 1.91%; (1.03% in males & 2.79% in females) & prevalence of overweight persons 11.48% (13.33% in males & 9.74% in females). As per NFHS-3, the percentage of women who are overweight or obese (BMI ≥ 25) was 28 % compared to 30% in Punjab and 26% in Delhi [1]. Among adults within the age group of 35-45 years around 72.9% were either overweight or obese in this study. In a study by Varghese et al., 41.7% in 35-40 years and 41.9 % in 40-45 years were obese or overweight . Overall 45% adults in this area had high WC (For men ≥ 90 cm and for women ≥ 80 cm). Higher proportion of women (50%) than men (35%) had high WC . For men Waist circumference ≥ 90 cm and for women ≥ 80 cm, were considered as high. Around 68% of adults had high WHR. Higher proportion of women (77%) had high WHR compared to 48% among men. Women had 3.6 times more risk of central obesity (high WHR) compared to males. Vijayakumar et al [7] reported the prevalence of central obesity (WHR > or = 0.80 [women] and > or = 0.90 [men]) was 85.6 percent in a study conducted in middle Kerala. In a study by Singh et al [8]. The overall prevalence of obesity (BMI ≥ 30) was 6.8% (7.8 vs. 6.2%) and of overweight was 33.5% (35.0 vs.32.0%, among women and men, respectively. The obesity prevalence was higher in Trivandrum (8.5%), Calcutta (7.1%) and Bombay (8.3%) compared to Moradabad (6.2%) among women, and among men it is higher in Trivandrum (7.4%) and Bombay (7.2%) compared to Nagpur (5.0%). The overall prevalence of subjects with BMI>23 kg/m2 was 50.8% and central obesity 52.6% in this five city study by Singh et al [8]. Among those who consume fast food the risk of obesity /overweight is 2.17 times higher.

Among adults with normal BMI <23, 29% had high WC than recommended for Asians (>90cm in males and >80 cm in women). Despite having lean BMI adult Indian has more chances of having abdominal obesity. Among Asian population, abdominal or central obesity is more common than obesity defined by BMI and health risks associated with overweight and obesity occur at lower levels of BMI. Obesity increases the insulin resistance and or reduces the number of insulin receptors on target cells. Abdominal obesity and visceral adiposity are the key determinants of insulin resistance, an important component of metabolic syndrome, the major CVD risk factor in all populations. At any given BMI, Indians may have a higher proportion of body fat, due to difference in body frame sizes and body proportions and thus an elevated risk of long term consequences of obesity like diabetes and CVD.

Conclusion

Overall prevalence of obesity & overweight in a rural population of Ahmednagar, Maharashtra was 40% and 24% respectively, as per new WHO BMI guidelines for Asians. Nearly three fourth (72%) of adults in the age group of 35-45 years were found to have BMI ≥ 23. Prevalence of central obesity is also very high. Even among those with normal BMI, central obesity is prevalent. Central obesity is a greater risk factor for development of type 2 DM and risk is related to both the degree and duration. The burden of obesity on health care system will be very high, due to its long term consequences. Primary prevention of obesity has to be recognized as a public health priority.

Action must be taken to integrate physical activity into daily life, not just to increase leisure time exercise. Awareness to reduce fast food consumption should be given high priority. Yoga can be used to maintain optimal weight of our country men and women. In addition to improving physical activity, yoga can help in preventing stress.

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A Study on Maternal Risk Factors and Preterm Neonates

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Abstract

Introduction: Factors that affect the state of lung development at birth include prematurity, maternal diabetes and genetic factors (white race, history of RDS in siblings, male sex). Thoracic malformations that cause lung hypoplasia, such as diaphragmatic hernia, may also increase the risk for surfactant deficiency. *Methodology:* The maternal and gestational variables studied were: Age (years), number of pregnancies, prior history of miscarriages, still births and premature deliveries; type of delivery (normal or caesarean); previous caesarean section, intercurrent clinical conditions observed during gestation – diabetes, hypertension, anemia, urinary infections at any point during pregnancy, syphilis, human immunodeficiency virus (HIV), toxoplasmosis, heart disease, hepatitis B, premature rupture of membranes (PROM) for longer than 18 hours, placental abruption *Results:* Maternal risk factors were present in 67% mothers which constitute about 67%. Among which Anemia (15%) and PROM (10%) has high incidence. PIH and previous history of LSCS constitute about 9% and 5% followed by Maternal Fever and younger age 9% & 4% . APH were found in 3 which constitute about 3%. BOH found in 2 mothers which accounts for about 2%. *Conclusion:* In the present study also PROM and anemia constitute the major maternal risk factor.

Keywords: Maternal Risk Factors; Preterm Neonates; PROM.

Introduction

After birth, infants with fetal lung structure and immature functional capacity are at greatest risk of respiratory distress need for oxygen and positive pressure ventilation and admission for intensive care. From 340/7 through 366/7weeks' gestation, terminal respiratory units of the lunge volve from alveolar saccules lined with both cuboidal type II and flat type Iepithelial cells (terminal sac period) to mature alveoli lined primarily with extremely thin type I epithelial cells(alveolar period) [1]. During the alveolar period, pulmonary capillaries also begin to bulge into the space of each terminal sac and adult pool sizes of surfacetant are attained. Functionally, this immature lung structure may be associated with delayed intrapulmonary fluid absorption, surfactant in sufficiency and in efficient gas exchange [1]. They pose resuscitation difficulties at birth, often followed by hyaline membrane disease, if associated with deficiency of pulmonary surfactant. Pulmonary aspiration and atelectasis are common [2].

Little is known about cardio vascular physiology and path biology in latepreterm infants; it is generally believed that structural and functional immaturity restricts the amount of cardiovascular reserve that is available during times of stress. Immature cardiovascular functional so may complicate recovery of the late-preterm infant with respiratory distress because of delayed ducts arteriosus closure and persistent pulmonary hypertension [3].

The primary cause of respiratory distress syndrome (RDS), also known as hyaline membrane disease, is in adequate pulmonary surfactant due to

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pretermbirth. The manifestations of the disease are caused by the resultant diffuse alveoli ate lactases, edema and cell injury. Subsequently, serum proteins that inhabit surfactant function leak into the alveoli. The increased water content, immature mechanisms for clearance of lung liquid, lack of alveolar-capillary apposition and low surface area for gas exchange typical of the immature lung also contribute to the disease. Significant advances made in the management of RDS include the development of prenatal diagnosis to identify infants at risk, prevention of the disease by antenatal administration of glucocorticoids, improvements in prenatal and neonatal care, advances in respiratory support and surfactant replacement therapy. As a result, the mortality from RDS has decreased. However, the survival of increasing numbers of extremely immature infants has provided new challenges and RDS remains an important contributing cause of neonatal mortality and morbidity [4].

Prenatal Risk Factors

1. Factors that affect the state of lung development at birth include prematurity, maternal diabetes and genetic factors (white race, history of RDS in siblings, male sex). Thoracic malformations that cause lung hypoplasia,such as diaphragmatic hernia, may also increase the risk for surfactant deficiency.
2. Factors that may acutely impair surfactant production,release or function include perinatal asphyxia in premature infants and cesarean section without labor. Infants delivered before labor starts do not benefit from the adrenergic and steroid hormones released during labor, which increase surfactant production and release. As a result, RDS may be seen in late preterm or early term infants delivered by elective cesarean section.

Antenatal corticosteroid therapy should be given to pregnant women 24 to 34 weeks gestation with intact membranes or with pretermrupture of the membranes (PROM) without chorioamnionitis, who are at high risk for preterm delivery within the next 7 days. Treatment at gestational ages <24 weeks is of questionable efficacy.

This strategy induces surfactant production and accelerates maturation of the lungs and their fetal tissues, resulting in a substantial reduction of RDS, intra ventricular hemorrhage (IVH), necrotizing enterocolitis and perinatal mortality. A fullcourse consists of two doses of betamethasone (12mgIM) separated by a 24-hourinterval, or four doses of dexamethasone (6 mg IM) at 12-hour intervals, although incomplete courses may improve out come. Contra indications to treatment include chorioamnionitis or other indications for immediate delivery [5].

A premature infant with RDS has clinical signs shortly after birth.These include tachypnea, retractions, flaring of the nasal alae, grunting and cyanosis.The classic radiographic appearance is of low volume lungs with a diffuse reticulo granular pattern and air broncho grams [6].

Methodology

The maternal and gestational variables studied were: Age (years), number of pregnancies, prior history of miscarriages, still births and premature deliveries; type of delivery (normal or caesarean); previous caesarean section, intercurrent clinical conditions observed during gestation–diabetes, hypertension, anemia, urinary infections at any point during pregnancy, syphilis, human immuno-deficiency virus (HIV), toxoplasmosis, heart disease, hepatitis B, premature rupture of membranes (PROM) for longer than 18 hours, placental abruption.

The neonatal variables studied were: Age at admission, days in hospital,sex, birth weight; gestational age (Calculated from modified Ballard's scoring); hypothermia/ hyperthermia (hypothermia: body temperature below 36^{o}C, hyperthermia: temperature above 37.5^{o}C); hypoglycemia (glucose below 40 mg/dL); hyperbilirubinemia requiring phototherapy/exchange transfusion; feed intolerance; respiratory pathologies – transient tachypnea of the newborn (TTN), hyaline membrane disease (HMD), pneumonia, sepsis,interventions done, deaths, rehospitalizations.

Inclusion Criteria

All late preterm babies ($34^{0/7}$ weeks to $36^{6/7}$ weeks) admitted to SNCU and postnatal wards for a period of Five months (September 2015 –February 2016).

Exclusion Criteria

1. Late preterm babies of parents who have not given consent.
2. Late preterm babies who had surgical conditions, congenital malformations, genetic disorders, metabolic disorders other than hypoglycaemia (suspected IEM), babies of multiple gestation.

Results

Maternal risk factors were present in 67% mothers which constitute about 67%. Among which Anemia (15%) and PROM (10%)has high incidence. PIH and previous history of LSCS constitute about 9% and 5% followed by Maternal Fever and younger age 9% & 4% . APH were found in 3 which constitute about 3%. BOH found in 2 mothers which accounts for about 2%. Diabetes and found in 1%. Maternal risk factor could not be elicited in 33 cases which constitute about33%. And 6 (6%)mothers had 2 or more identifiable risk factors.

Regarding mode of delivery, vaginal delivery was conducted in 81 neonates which accounts for 81%. 19 neonates were born through LSCS which accounts for 19%.

Regarding birth weight, 17 neonates were born with birth weight between 2 and 2.5kg which constitute about 17%. 1 neonate were born with birth weight above 2.5 kg which constitute about 1%. 68 neonates were born with birth weight between 1.5 and 2 kg which constitute about 68%. 17 neonates were born with birth weight of <1.5 kg which constitute17%.

Table 1: Maternal risk factor

Maternal risk factor	No. of patients (n=203)	%
No	33	33
Yes	67	67
1.PROM	10	10
2. Previous LSCS	5	5
3.Anaemia	15	15
4.PIH	9	9
5. Fever	9	9
6. APH	3	3
7.Younger age	4	4
8 BOH	2	2
9.Diabetes	1	1
10.Elderlyprimi	3	3
11.2 or more risk factors	6	6

Table 2: Mode of delivery

Mode of delivery	No. of patients	%
NVD(Normal Vaginal delivery)	81	81
LSCS	19	19
Total	**100**	**100**

Table 3: Birth weight (kg)

Birth weight	No. of patients	%
<1.5	14	14
1.5-2	68	68
2-2.5	17	17
>2.5	1	1
Total	100	100

Discussion

Maternal risk for preterm was elicited in 67 cases which accounts for about 67%. There were no recorded indication In 33 mothers which constitute about 33%. Among risk factors studied Anemia & PROM constitutethemajor one's of 15% and 10% respectively followed by PIH(9%) & more than two risk factors respectively.

Reddy et al. had studied the "Delivery indications of late-preterm gestations" in 2009 and he categorized delivery indications as follows: (1) maternal medical conditions; (2) obstetric complications; (3) major congenital anomalies; (4) isolated spontaneous labor: vaginal delivery without induction and without associated medical/obstetric factors; and (5) no recorded indication. Of the 292 627 late-preterm births, the first 4 categories (those with indications and isolated spontaneous labor) accounted for 76.8%. The remaining 23.2% (67,909) were classified as deliveries with no recorded indication. He concluded

that a total of 23% of late preterm births had no recorded indication for delivery noted on birth certificates and patient factors may be playing a role in these deliveries. It is concerning that these infants had higher mortality rates compared with those born after spontaneous labor at similar gestational ages [7].

In this study there were no recorded indications in 33% of the neonates which is inpar with Reddyetal. Prolonging pregnancy to the maximum safest gestation will result in decrease in morbidities.

Tucker J Metaldid a study, "Etiologies of preterm birth in an indigent population: is prevention logical expectation? " The study results were compared with births < 34 weeks, late preterm births are more likely to be the result of spontaneous idiopathic preterm labor or PPROM than medical or pregnancy indications [8]. It has been estimated that the relative distribution of etiologies of preterm birth < 34 weeks' gestation is 30% indicated, 30% PPROM, and 40% spontaneous preterm labor. For late preterm births, the relative distribution of etiologies changes to 20% indicated, 25% PPROM, and 55% preterm labor. As such, larger proportion of late preterm births are due to spontaneous preterm labor (two- thirds) compared with PPROM (one-third) [4].

In the present study also PROM and anaemia constitute the major maternal risk factor (15%) which is in par with the above study and spontaneous preterm labor seen in 5%.

Laughon et al. in 2010 reported similar findings, showing that a consider able number of preterms are born by caesarean with no record of any indication for caesarean delivery, which suggests that they are potentially avoidable. In that, 15,136 late preterm infants were studied and categories the precursors as "spontaneous labor," "premature rupture of the membranes (preterm PROM),"indicated" delivery and" unknown. "The study concluded PROM as the major precursor of latepreterm delivery constituting about 32.3% followed by "indicated" (obstetric, maternal, or fetal condition) and spontaneous labor which constitute 31.8% and 29.8% respectively. In 6.1% precursor were unknown. They concluded that one in 15neonates delivered late preterm for "soft" or elective precursors [9]. In this study also 33% of late preterm were with unknown precursor which is comparable with the above study. About 81 neonates had vaginal deliveries which constitute about 81%. LSCS was done in 19 neonates which constitute19%.

Jean-Bernard Gouyon et alin 2010 did a study, Neonatal outcome associated with singleton birth at 34–41 weeks of gestation. In this study they found vaginal delivery was more compared to Caesarean section which is inpar with the present study. They also found gestational age was positively correlated with vaginal delivery and negatively correlated with emergency caesarean section [10].

Conclusion

Prolonging pregnancy to the maximum safest gestation will result in decrease in such morbidities. Further studies in the physiology, developmental maturity that are specific to latepreterm infants are required.

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Clinical Profile of Late Preterm Neonates at Tertiary Care Hospital

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Abstract

Introduction: During the past few decades, preventive and therapeutic interventions focused primarily on low birth weight infants and deliveries occurring at less than 34 weeks. Many clinicians have become increasingly comfortable with births in late preterm gestations and many seemingly choose elective delivery well before 39 to 40 weeks of gestation, mistakenly believing that these neonates may be as physiologically and metabolically mature as term new borns. *Methodology:* Data were collected from infants and mothers medical records and supplemented with additional information collected at discharge using a structured form covering the variables of interest. Variables relating to the mothers and their infants were analyzed. *Results:* Regarding gestational age, 18 neonates were admitted between the gestational age of $34^{0/7}$ to $34^{6/7}$ weeks who constitute about 18%. 16 neonates were admitted between the gestational age of $35^{0/7}$ to $35^{6/7}$ weeks who constitute about 16% and 66 neonates were admitted between the gestational age of $36^{1/7}$ to $36^{6/7}$ weeks who constitute 67%. *Conclusion:* Majority of babies were admitted within first three days of life.

Keywords: Preterm Neonates; Gestation; Low Birth Weight.

Introduction

With 4 million births annually in the United States, a 12.5% preterm birth rate computes into a staggering figure of one preterm infant born each minute. It is also note worthy that in all preterm gestations, there has been an increase in cesarean births and induced deliveries [1]. This is concerning because there is a large proportion of induced births in late preterm gestations with documented etiology. Some explanations for the increasing preterm birth are increasing proportion of pregnant women older than 35 years of age, medically indicated deliveries secondary to better surveillance of the mother and the fetus, attempts to reduce stillbirths and stress from a variety of sources. However nationwide epidemiologic studies are needed to inform the etiology of increasing preterm births, especially in the late preterm gestations [2].

During the past few decades, preventive and therapeutic interventions focused primarily on low birth weight infants and deliveries occurring at less than 34 weeks. Many clinicians have become increasingly comfortable with births in latepreterm gestations and many seemingly choose elective delivery well before 39 to 40 weeks of gestation, mistakenly believing that these neonates may be as physiologically and metabolically mature as term new borns. There is now a growing awareness with regard to late preterm birth due to the un anticipated rate of complications this group has demonstrated. Neonates born between 34 and 36 weeks of gestation (latepreterm or near term births) comprise 71% of all preterm births in the United States. Latepreterm neonates have significantly higher rates of morbidity and mortality relative to those born at term (37-42 weeks). In addition to higher risks for serious health complications, the mortality rate for late preterm infants is 3-fold higher than that for term

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infants (7.7 vs 2.5 per 1000 live births) [3].

The mechanisms initiating normal labour are not clearly understood and muchless are known about the triggers that initiate labour before term. There may be spontaneous onset of premature labour or it may be induced by the Obstetrician to safe guard the interests of the mother or baby [4].

The cause of premature on set of labour is uncertain in most instances. The known causes include poor socio-economic status, low maternal weight, chronic and acute systemic maternal disease, antepartum hemorrhage, cervical incompetence, maternal genital colonization and infections, threatened a abortion, acute emotional stress, physical exertion, sexual activity, trauma, bicornuate uterus, multiple pregnancy and congenital malformations.

Premature births are relatively common among very young and unmarried mothers. Past history of preterm birth is associated with 3 to 4 times increased risk of prematurity in the sub sequent pregnancies [4].

The labour is often induced before term when there is impending danger to mother or fetal life in utero e.g.maternal diabetes mellitus, placentaldys function as indicated by unsatisfactory fetal growth, eclampsia, fetal hypoxia, antepartum hemorrhage and severe rhesus's-immunization [4].

The Obstetrician faces many challenges while managing women in labour in any preterm gestation. These include balancing the benefits of immediate delivery against the risks of prematurity and assessing the benefits of expectant management versus the potential risk of compromising maternal and fetal health. Furthermore, there are well known, medically indicated causes of preterm births, such as placental abruption, placenta previa, bleeding, infection, hypertension, multiple pregnancy, preeclampsia, idiopathic preterm labor, premature rupture of membranes, and intrauterine growth restriction [2].

However, with the exception of multiple pregnancies, there is no indication that the prevalence of other conditions are on the increase. Thus, some experts contend a sizable number of late preterm births can be prevented; however more studies are needed to substantiate this claim [2].

The reason for the increase in late preterm births during the last decade is not well understood. One hypothesis is that it may be attributable, in part, to increased use of reproductive technologies and as a result, an increase in multifetal pregnancies. Another hypothesisis that advances in Obstetric practice have led to an increase in surveillance and medical interventions during pregnancy. As a result, fetuses considered to be at risk of still birth, including those with intrauterine growth restriction, fetal anomalies and intrapartum asphyxia, may be identified earlier, which results in more deliveries at 34 to 36 weeks' gestation. Forexample, between 1989 and 2003, the use of electronic fetal monitoring and prenatal ultrasonography increased substantially from 68.1% to 85.4% and 47.6% to 67%, respectively. Rates of labour induction and cesarean delivery also increased during the last decade. It is important to note, however, that the increased intensity of care provided to pregnant women has been accompanied by significant reductions in still births, perinatal mortality and births beyond 40 weeks' gestation [5].

To date, limited studies have addressed the etiology of late preterm births. Reddy et al categorized the etiology of late preterm deliveries into five groups: maternal medical conditions, Obstetric complications, major congenital anomalies, isolated spontaneous deliveries and no recorded indications, which accountedfor14%, 16%, 1%, 49% and 23.2% of all deliveries respectively [6].

Laughon et al reported that spontaneous labor, preterm premature rupture of membranes and indicated deliveries each accounted or about 30%o flat preterm births. These two studies revealed three aspects. Firstly, medically indicated elective cesarean sections (CSs) were responsible for the majority of all latepreterm deliveries; secondly, varied neonatal morbidities and mortalities depended upon the indications for delivery; and thirdly, a certain proportion of deliveries with unknown indications were likely patient scheduled CS and thus potentially avoidable [7].

No consensus has yet been reached on the contributing factors of the increase in latepreterm births.Available data have suggested medically indicated deliveries and patient driven factors were responsible for the increase of late preterm newborns. Because the actual indication for delivery is recognized as a determination neonatal outcome, more attention should be devoted to examine the etiology of latepreterm births [6,7].

Methodology

Details regarding maternal risk factors were collected by detailed history taking and the medical records with them. The infants in the sample were followed throughout their stay in the SNCU and postnatal wards, up until hospital discharge. Data were collected from infants and mothers medical

records and supplemented with additional information collected at discharge using a structured form covering the variables of interest. Variables relating to the mothers and their infants were analyzed.

The maternal and gestational variables studied were: Age (years), number of pregnancies, prior history of miscarriages, still births and premature deliveries; type of delivery (normal or caesarean); previous caesarean section, intercurrent clinical conditions observed during gestation – diabetes, hypertension, anemia, urinary infections at any point during pregnancy, syphilis, human immunodeficiency virus (HIV), toxoplasmosis, heart disease, hepatitis B,premature rupture of membranes (PROM) for longer than 18 hours, placental abruption.

The neonatal variables studied were: Age at admission, days in hospital, sex, birth weight; gestational age(Calculated from modified Ballard's scoring); hypothermia/ hyperthermia (hypothermia: body temperature below 36°C, hyperthermia: temperature above 37.5 °C); hypoglycemia (glucose below 40 mg/dL); hyperbilirubinemia requiring phototherapy/exchange transfusion; feed intolerance; respiratory pathologies – transient tachypnea of the newborn (TTN), hyaline membrane disease (HMD), pneumonia, sepsis,interventions done, deaths, rehospitalizations.

Incluson Criteria

All late preterm babies ($34^{0/7}$ weeks to $36^{6/7}$ weeks) admitted to SNCU and postnatal wards for a period of Five months (September 2015 –February 2016).

Exclusion Criteria

1. Late preterm babies of parents who have not given consent.
2. Late preterm babies who had surgical conditions, congenital malformations, genetic disorders, metabolic disorders other than hypoglycaemia (suspected IEM),babies of multiple gestation.

Results

351 late preterm neonates were admitted during the study period, out of which 100 babies met the inclusion criteria.

Age of admission varies from day 1 of life to 30 days of life. Majority of babies were admitted within first three days of life. 88 babies were admitted within first three days of life which constitute 88%. 4 babies' were admitted between day 4 and day 6 of life which constitutes about 4%. 4 babies were admitted between 7 to 10 days of life which constitute about 4%. 2 children were admitted between 11 to15 days of life which constitute about 2%. 1 child was admitted at day 16 of life which constitute about 1%.

Out Of the 100 neonates, 48 were male who constitute about 48% and 52 neonates were female who constitute 52%. Sex distribution showed female predominance.

Regarding gestational age, 18 neonates were admitted between the gestational age of $34^{0/7}$ to $34^{6/7}$ weeks who constitute about 18%. 16 neonates were admitted between the gestational age of $35^{0/7}$ to $35^{6/7}$ weeks who constitute about 16% and 66 neonates were admitted between the gestational age of $36^{1/7}$ to $36^{6/7}$ weeks who constitute 67%

Table 1: Age distribution of neonates studied

Age at admission (days)	No. of patients	%
1-3	88	88
4-6	4	4
7-10	4	4
11-15	2	2
15-20	1	1
Total	100	100

Table 2: Gender distribution of neonates studied

Gender	No. of patients	%
Female	52	52
Male	48	48
Total	100	100

Table 3: Gestational age in weeks

Gestational age	No. of patients	%
$34^{0/7}$ to $34^{6/7}$	18	18
$35^{0/7}$ to $35^{6/7}$	16	16
$36^{0/7}$ to $36^{6/7}$	66	66
Total	100	100

Discussion

Late preterm infants are at high risk for neonatal morbiditiesespecially neonatal hyperbilirubinemia requiring phototherapy, respiratory morbidity, need of mechanical ventilation, sepsis, hypoglycemia. Length of stay, mortality rate and rate of rehospitalizations were high. This implies that extreme caution should be taken while discharging these babies. It is of utmost importance to counsel parents regarding the morbidities that their babies can have and to stress to them the importance of monitoring feeding, weight gain, jaundice and apnea.

Prolonging pregnancy to the maximum safest gestation will result in decrease in such morbidities.

The study comprised of 100 late preterm neonates. The frequency of preterm births is increasing in many countries and this increase is mainly due to rise in late pre term births. There is only limited published data from India related to morbidities of late preterm neonates. Many reasons were proposed to explain this increasing trend including increased surveillance of the mother and fetus, increasing maternal age and reproductive technologies which are associated with multiple pregnancies. It is suggested that as a result of increased surveillance, fetuses considered to be at risk of stillbirth, including those with intrauterine growth restriction, fetal anomalies, and intra partum asphyxia may be identified earlier, which results in more deliveries at 34 to 36 weeks gestation [8].

This study demonstrates the importance and magnitude of the risks of inter current conditions to which infants born at $34^{0/7}$ to $36^{6/7}$ weeks gestation are subjected.

In this study Female predominance was observed, with 52% comprising male babies and female babies constitute about 48% which is comparable with the study conducted by AshishJaiswal et al [9]. In their study female sex constitute about 45.5%. Male predominance is seen in another study conducted by Jean-Bernard Gouyon et al [10], where male babies constituted about 55.4%.

Majority of the neonates were admitted within 3 days of life. About 88 neonate were admitted which accounts for about 88%.

Treating latepreterm infant as almost term and almost normal infants should be avoided. The concept of late preterm babies as almost full term infants means that they are discharged prematurely, following the routine protocols set out for full term babies. Discharging these infants before 48 hours precludes the opportunity of identifying morbidities early enough to allow timely intervention. It is not there for surprising that these infants have a much higher rate of hospital read mission. It is important to explain to parents the vulnerabilities to which their children are subject to and to stress to them the importance of monitoring feeding, weight gain, jaundice and apnea. These inter current conditions are frequently responsible for a hospital visit within 48 hours of discharge It is therefore important that further studies be conducted to:

a. Establish and evaluate strategies, routines and protocols for premature interruption of pregnancy that are more rigorous and are based on scientific evidence, there by reducing the number of premature births and
b. Develop Obstetric protocols that increase the precision of methods for estimating gestational age, such as, for example, routine ultrasound in the first trimester, which is important to decision-making when considering interrupting a pregnancy before full term.

Another intervention that merits greater study is the possibility of using antenatal corticosteroid after 34 weeks to reduce respiratory pathologies and prevent a significant number of deaths in this group of neonates [2].

Conclusion

It is of utmost importance to counsel parents regarding the morbidities that their babies can have and to stress to them the importance of monitoring feeding, weight gain, jaundice and apnea.

Prolonging pregnancy to the maximum safest gestation will result in decrease in such morbidities.

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Clinical Study of Neonatal Septicemia with Reference to Early Indicators of Sepsis in NICU, PIMS

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Absract

Neonatal septicaemia is a major cause of morbidity and mortality in new born infants. *Back ground and objectives:* to study the incidence, predisposing factors, clinical profile, out come, early indicators of correlation with all clinical aspects and antibiotic sensitivity pattern of neonatal septicaemia. *Materials and Methods*: The 50 neonates who are showing the well documented signs of septicaemia are included in this study. *Results*: culture was bacteriologically positive in 34% cases. Ciprofloxacin had maximum sensitivity 88.2%. Leucopoenia ≤5000/cmm had sensitivity of 47% specificity of 66.67% and ppa of 42.11%,toxic granulation had 70.56% sensitivity, 63.65% specificity and 50% ppa. B/n>0.2 had 88.2% sensitivity 62.4% ppa. m-ESR had sensitivity of 70.56%, specificity of 84.84%, ppa of 70.5%, c-reactive protein had 88.2% sensitivity and 87.8% specificity and 78.95%ppa. Case fatality rate was 28%. *Conclusion:* Clinical features of neonatal septicaemia are non specific and vague. Sepsis screen had good sensitivity, specificity and ppa. combination of tests increase the specificity and ppa. An an individual test c- reactive protein has highest sensitivity.

Keywords: Neonates; Septicaemia; Outcome.

Introduction

Neonatal septicaemia is defined as a bacterial infection documented by a positive blood culture in the first four weeks of life. Systemic bacterial infection during the first month of life have remained a major cause of infant morbidity and mortality.

The early diagnosis of neonatal septicaemia still poses great difficulties. Early clinical symptomatology of neonatal septicaemia is mimicked by lot of other disorders affecting the newborn. It is a major cause of morbidity and mortality and it accounts for half of the neonatal deaths in this country. The overall incidence of neonatal sepsis varies between 1-8 cases/100 live births. Neonatal sepsis can be divided into 2 subtypes depending upon whether the onset of symptoms is during the first 72 hours of life or later. Although the term early onset sepsis had been used to refer to neonatal infection occurring as late as one week of age, it should be restricted to those infections with a perinatal pathogenesis, the usual onset of which occur within 72 hours. Early–onset sepsis is caused by organisms prevalent in genital tract or in the labour room. Ascending infection, transplacental haematogenous spreads are important mechanisms of early onset sepsis.

After the birth the baby is exposed to the environment contaminated with micro organisms, which start setting or colonising at various places. The organisms enter the body through the umbilicus, skin or mucosa. Due to poor immunological defence of the new born, even local infections tend to become generalised. Infections are more commonly met with preterm and low birth weight babies. To prevent serious morbidity and mortality caused by untreated or lately treated neonatal septicaemia, it is important that the diagnosis is made early and the treatment

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started as easily as possible. Even though the positive blood culture is diagnostic of neonatal septicaemia, the technique of blood culture is time consuming that demands a well equipped laboratory and has a success rate of only 40%, therefor the blood culture has its own limitation.

Early tearment with rational antibiotic therapy is possible with the help of certain indirect markers such as leucopenia, toxic granules, band form to neutrophil ratio, micro–esr and c-reactive protein. This investigation excercise is collectively known as sepsis screen. The early diagnosis of neonatal sepsis by clinical examination is vital. In the presence of predisposing factors, early clinical suspicious coupled with sepsis screen will detect neonatal septicemia earlied, which will enable the clinician to treat the infection timely and adequately,which in turn will help to reduce the neonetal morbidity and mortality.

Aims and Objectives

- To study the incidence and predisposing factors of neonatal septicemia.
- To study the clinical profile and outcome of septicemia.
- To study the early indicators and correlation with all clinical aspects neonatal septicemia.
- To study the bacteriology and antibiotic sensitivity pattern of neonatal septicemia.

Material and Methids

This study was conducted in prathima institute of medical sciences, nagunoor. 50 neonates below the age of 28 days with clinical suspicion of neonatal septicemia were included in this study. Neonates admitted in our hospital from out patient depatment and neonates born in same hospital were included in this study group. After admission detailed history was taken and through clinical examination was done. Consent was taken from parents. Institutional ethical commity permission taken. Results were analysed on different parameters.

Results

This study conducted our 50 neonates. Out of 50, males are 33 (66%), females are 17(34%).

Early onset of septicemia was present in 34 (68%) cases, late onset of septicemia was seen in 16 (32%) cases (Table 1). Neonatal risk factors like low birth weight and prematurity were present in 68% and 60% cases respectively. Maternal risk factors observed were prolonged rupture of membranes >18hrs (30%), home delivery 24%, poor maternal health and hygiene of genital (58%). In 86 of cases there was one or more predisposing factor present.

Common clinical manifestation of neonatal septicemia were refusal of feeds (56%), temperature abnormality (46%), sclerema (44%). jaundice (42%), pallor (36%) not doing well (24%), rash (20%) and convulsion (16%). Culture was bacteriologically positive in 17 (34%) cases, negative in 33(66%) cases. Isolated organism were e.coli 7(42.5%), klebsiella 4(23.5%), staphylo coccus aureus 3(17.6%), pseudomonas 2 (11.7%), proteus 1(5.7%). In this gram negative organism were detected in 14(82.3%) cases, gram positive were in 3 (17.7%) cases (Table 2)

Toxic granulation present in 12 (70.56%) of 17 bacteriologically positive cases (Table 3) Positivity and negativity of combined test shown in Table 4. White blood cell counnt Sensitivity was 47%, specificity was 66.67%. Positive predictive accuracy of the test 42.11% (Table 5). Outcome of the patient with various factor depicted in Table 6.

Table 1: Distribution of cases

Age of onset	Maturity		Total	Birth weight	
	Pretem	Term		≤ 2500gms	> 2500gms
≤ 7 days	19	34	34	20	14
>7 days	11	16	16	14	2
total	30	50	50	34	16

Table 2: Distribution of isolated organism

Gram Staining	Age of onset		Total	Birth Weight	
	≤ 7 days	>7 days		≤ 2500gms	> 2500gms
Gram negative	7	1	14	10	4
Gram positive	1	2	3	2	1
total	8	9	17	12	5

Table 3: Different test profile

		Culture		Total
		Bacteriologically positive cases-17	Bacteriologically negative cases-33	
Wbc count	≤ 5000/cmm	8 (47%)	11(33.33%)	19
	>5000/cmm	9(53%)	22(66.67%)	31
Toxic	Present	12(70.56%)	12(36.37%)	24
granulation	Absent	5(29.44%)	21(63.63%)	16
B/N	B/N ≥ 0.2	15 (88.2%)	12(36.37%)	24
	B/N < 0.2	2(11.8%)	21(63.63%)	26
m-ESR	≥ 15mm at the end of 1st hr	12(70.56%)	5(15.16%)	17
	< 15mm at the end of 1st hr	5(27.4%)	28(84.84%)	33
c- reactive	Positive	15 (88.2%)	4(12.2%)	19
protein	negative	2(11.8%)	29(87.8)	31

Table 4: Positivity and negativity of combined tests

		Culture		Total
		Bacteriologically positive-17 cases	Bacteriologically negative-33 cases	
Toxic granulation + c-reactive protein	Positive	10(58.8%)	3(9.11%)	13
	negative	7(41.2%)	30(90.9%)	37
c- reactive protein +m ESR	Positive	11(64.68%)	2(6.07%)	13
	negative	6(35.32%)	31(93.93%)	37
Toxic granulation +m-ESR	Positive	10(58.8%)	4(12.13%)	14
	negative	7(66.7%)	29(87.87%)	36
c- reactive protein + Toxic granulation +m-ESR	Positive	8(47.04%)	2(5.07%)	9
	negative	9(52.96%)	31(93.93%)	41

Table 5: Sensitivity and specificity of different tests

Test	Sensitivity	Specificity	Positive Predictive Accuracy
WBC Count ≤ 5000cmm	47%	66.67%	42.11%
B/N ≥ 0.2	88.2%	63.63%	62.4%
Toxic Granulation	70.56%	63.65%	50%
M-ESR>Mm At The End Of 1st Hr	70.56%	84.84%	70.5%
C-Reactive Protein	88.2%	87.8%	78.95%
C-Reactive Protein+ Toxic Granulation	58.8%	90.9%	76.9%
C-Reactive Protein+ M-ESR	64.68%	93.93%	84.6%
Toxic Granulation+ M-ESR	58.8%	87.87%	71.6%
C-Reactive Protein+ Toxic Granulation+ M-ESR	47.04%	93.93%	88.8%

Table 6: Outcome of the patient with various factor

Factors		Outcome		Total
		Death-14	Survivals-36	
maturity	preterm	9(64.26%)	21(58.5%)	30
	Full term	5(35.74%)	15(41.5%)	20
Age of onset	≤ 7days	10(71.4%)	24	34
	>7days	4(28.6%)	12	16
Birth weight	≤ 2500gm	9(64.26%)	25	34
	>2500gm	5(35.74%)	11	16
culture	Bacteriologically positive	10(71.4%)	8	18
	Bacteriologically positive	4(28.6%)	28	32
Gram staining	Gram negative	9(90%)	5(71.43%)	14
	Gram Positive	1(10%)	2(28.57%)	3

Discusssion

This study was conducted in pims,nagunoor our 50 neonates below the age of 28 days with clinical suspicion of neonatal seticemia were included in this study by considering clinical profile, sepsis screen, outcome of neonatal septicemia.

Out of 50 males were 33 female were 17. Nelson [1] stated that males have an approximately 2 fold higher incidence of sepssis than females. H. David [2] wilson

stated that increased incidence of sepsis neonatorum in male infants in probably related to the higher incidence of congenital anomalies of the urinary tract in the the males, resulting primary urinary tract infection and secondary sepsis.

Early onset septicemia is ≤ 7 days was present in 34 cases (68%) and onset septicemia was >7 days was present in 15 cases (32%). In our study the early onset septicemia was more common because of maternal risk factors like prolonged rupture of membranes, home delivery, h/o of intrapartum maternal infection, poor maternal health and hygiiene of genital and neonatal risk factors like prematurity and low birth weight.

According to birth weight low birth weight i.e ≤ 2500 gm was present in cases (68%). These findings were cosistant with other studies. Nellian et. al [3], N mehrotra et al, piyush gupta et. al, agarwal et.al, khatua et al. And koutociby et, al. observedthat low birth weight new born have highter incidence of neonatal septicemia. N.sinha et. al [4] observed that babies with low birth weight predominated (64.9%).

In 50, 30 cases were preterm babies (60%). Anad et. al [5] observed that 62% preterm babies were affected. Khatua et, al [6] observed that out of 92 babies with neonatal septicemia 58 were preterm in 56.52%. Higher incidence of many complication of labour and resuscitation are more common in preterm babies than full term neonates. Preterm babies were relatively immuno- compromissed than immuno inexperienced. These factors predispose them to infection. Common neonatal predisposing factors detected in neonatal septicemia were prematurity (60%) and low birth weight (68%). Nelson [1] and cloherty [7] stated that the prematurity and low birth weight are the most important predisposing factors in neonatal septicemia.Common maternal factors observed were poor maternal health and hygiene of genitals (58%), prolonged rupture of membranes (31%), home delivery (23%) premature rupture of membranes(15%), h/o intrapartum maternal infection (9%). Udani et. al. And kishoret. al have reported high incidence of vertical trasmission and sepsis in babies born to mothers with prolonged rupture of membrane. Anand et. al [5] observed prolonged rupture of membranes in 29.3% of cases. N. mehrotra [8] noted three fold increase in the incidence of sepsis after prolonged rupture of membranes. James C. Overall et. al [9]. Observed that maternal infection, particularly of the uterus and urinary tract also significantly predisposes to neonatal infection. zilliacus and totterman noted a more than 6 fold grater incidence of internal infection in neonates born with mother with urinary tract infection at the time of delivery than in onnes born to mother without such infection.

In our study resuscitation after birth (17%) was observed as one of the important factor in neonatal septicemia. Dawodu et al [10] found that requirement of mechanical ventilation was important risk factor. Agarwal et. al [11] found that birth asphyxia was common predisposing factor. Motor et. al [12] Observed that mechanical ventilation for >5 days was significantly associated with neonatal sepsis. Mucosal abrasions or cutaneous defects associated associated with birth defects, fetal monitoring obstretical manipulation and/or vigorous resuscitation predispose to bacterial invasion and infection. Similarly the use of indwelling catheters. Fanaroff [13] atated that asphyxiated infants requiring resuscitative procedures including mechanical ventilation and catherization are at high risk of developing sepsis.

Commonly observed clinical manifestation were refusal to feeds (56%), temperature abnormality (47%), clerema (45%), jaundice (41%) pallor (36%) not doing well (24%), rash (21%) and convulsions (17%). Khatua et al [6] Observed that refsual of feeds, lethargy,diarrhea, temperature abnormality, abdominal distension, jaundice and vomiting were most common presenting features. Mishra et. al [14] observed that common clinical presentation were jaundice, lethargy, refusal of feeds, vomiting and respiratory distress.The clinical features of neonatal septicemia are non specific and may be clinical features of neonatal septicaemia are non specific and may be clinically indistinguishable from those occurring in non infectious conditions during neonatal period.

The culture was positive in 17 cases (34%). Gupta et al [15]. Observed culture positivity rate of 33%. Although blood culture are normally the basis for a diagnosis of bacterial infection the bacteremic phase of the illness may be missed by poor timing blood sample size so also before drawing blood sample for culture the patient may be treated with some parenteral antibiotic by private practioners or other hospital. Due to this the blood culture have loe sensitivity. Various organisms isolated in 17 culture positive cases were E.coli (42.5%), Klebsiella 4 (23.5%), staphylococcus aureus (17.6%), pseudomonas (11.7%) proteus (5.7%). N. Mehrotra [8] observed that e.coli were the most commonest group of organism isolated. similar observation have been made by Smith et. al [1], pseudomonas, proteus and klebsiella were the other organisms frequently found. In our study gram negative organisms were detected in 14 cases (82.3%). Our findings are consistent with others of Mathur et

al [16]. (66.5%) and khatua et al [6] (76.3%).In this study gram negative organisms were common cause of early onset of septicaemia. Our study consistant with j.n mishra et al study.he observed that early onset of septicaemia was present in 71.7% cases due to gram negative bacteria.In our study gram negative septicaemia was more common in low birth weight babies (83.3%). Our finding are consistant with Mishra et. al [14].

In this study leucopenia had sensitivity of 47% specificity of 66.67% and positive predictive accuracy of 42.11%. This is nearer to Namedo et. al [17] they observed that leucopenia had sensitivity of 44%,specificity of 69% and positive predictive accuracy of 48%. Unfortunately the positive predictive value of an abnormal wbc count is poor. this is not surprising since many non-infectious conditions can be associated with an abnormal neonatal wbc count.thus the initial wbc with differential cell count may not be helpful in the decision to initiate antibiotic therapy for an asymptomatic new born infant with indentified risk factor for sepsis. Nevertheless it is common practice to perform these tests as a part of the immediate post natal assessment of the "at risk" infant. In our study toxic granulation had 70.56%, sensitivity 63.65% specificity and 50% positive predictive accuracy. Our studies are consistant with Namedo et al [17]. They observed that toxic granulation had 80% sensitivity 70 specificity and 69 % positive predictive accuracy.In our study band –total neutrophil ratio had sensitivity (88.2%) specificity (63.63%) and positive predictive accuracy of (62.4%) our observations are consistent with Namedo et al [17]. They observed sensitivity of B/N ratio 82%. In our study micro–ESR test had sensitivity of 70.56%, specificity of 84.84% and positive predictive accuracy of of 70.5%. Our observations consistant with Parida et. al, they observed that m-ESR had 71% sensitivity, 73.3% specificity and 71.4% positive predictive accuracy. In this study C-reactive protein test had 88.2% sensitivity, 87.8% specificity and 78.95% positive predictive accuracy.our study consistant with Singh et. al [18] where 80% sensitivity, 91% specificity and 92% positive predictive accuracy present. In our study it was observed that when two on more tests were combined specificity and positive predictive accuracy were increased while sensitivity was decreased than the individual test.our study observations are consistant with Mishra et. al [17]. where the positive predictive accuracy and specificity of two test combination was higher than individual test at the cost of sensitivity.

In our study case fatality rate was 28%. The mortality was higher in preterm babies.this was due to poor defences against bacterial infections. In this study mortality was higher in early onset septicaemia. Our observations are consistent with Mathur et, al [20]. Where the mortality was 64.5% when the onset of illness was early. In this study mortality was higher in low birth weight babies.

Our observations are consistent with mishra et al [14]. where the mortality was 70%. In this study mortality was higher in gram negative septicemia. Our observations are consistent with khatue et al [6]. where the mortality was 78.5% in gram negative septicemia. one major factor for high mortality rates in gram negative septicaemia is probably the emergence of drug resistant strains.

Conclusion

1. Clinical features of neonatal septicemia are non specific, vague and may be clinically indistinguishable fro those occuring in noninfectious condition during neonatal period.
2. Male, preterm and low birth weight neonates are more prone for septicemia.
3. Early onset septicemia is more common than late onset septicemia.
4. Prolonged rupture of membranes, home delivery, poor maternal health and hygiene of genitals predispose neonatal to infection.
5. Gram negative septicema is more common than gram possitive septicemia
6. Gram negative organisms are common cause of early onset septicemia.
7. Gram negative septicemia is common in low birth weight babies.
8. Sepsis screen has good sensitivity,specificity and positive predictive accuracy and is a valuable aid in early diagnosis of neonatal septicemia.
9. Sepsis screen is simple, cheap, less time consuming and easy to perform even at bedside.
10. As an individual test c-reactive protein has highest sensitivity, specificity and positive predictive accuracy and is a sensitive and responsive indicator of neonatal sepsis.
11. Combination of tests increses the specificity and positive predictive accuracy.
12. Mortality is higher in preterm and low birth weight babies.
13. Mortality is higher in early onset septicemia and gram negative septicemia.

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Aetiology and Clinical Profile of Children with Hepatomegaly in Pediatric Age Group

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Abstract

Introduction: Liver disease in pediatric age group is one of the most significant causes of morbidity and mortality and includes a broad spectrum of disorders such as infections, developmental abnormalities, metabolic and neoplastic disorders that finally results in hepatic dysfunction and cirrhosis [1] and may recover fully. *Objective:* 1)To study the clinical profile of hepatomegaly in pediatric age group. 2)To identify etiological spectrum hepatomegaly in pediatric age group. *Material and Methods:* A prospective study will be carried out during 01.12.2014 to 31.05.2016 in 100 patients of pediatric age group presenting with hepatomegaly admitted in Navodaya Medical College Hospital Raichur. All the pediatric patients (birth – 18 years) admitted with hepatomegaly, (defined clinically) with span more than normal for age. The patients will be evaluated clearly based on history, clinical examination and requisite laboratory parameters to find out the cause of hepatomegaly. This study will be conducted as a prospective Clinical study, wherein written informed consent will be taken prior to the investigation after detailed information given to the guardians regarding the study. Children with hepatomegaly will be screened through history, detailed examination and correlated through lab investigations. *Results:* Male predominance was seen in our study.Maximum incidence of hepatomegaly was seen between 1 to 4 year age group (34%). Majority of the cases had mild hepatomegaly (64%). Commonest cause of hepatomegaly was infections. Fever was the most common symptom associated with hepatomegaly. Splenomegaly was the most common sign associated with hepatomegaly. *Conclusion:* Infection is the most common cause of hepatomegaly in our study. Male preponderance was seen in majority of the cases who had hepatomegaly and belonged to pre school age group.

Keywords: Hepatomegaly; Anemia**.**

Introduction

Liver disease in pediatric age group is one of the most significant causes of morbidity and mortality and includes a broad spectrum of disorders such as infections, developmental abnormalities, metabolic and neoplastic disorders that finally results in hepatic dysfunction and cirrhosis [1] and may recover fully.

In developing tropic and sub-tropic countries hepatomegaly in pediatric age group is a common problem in medical practice.

Hepatomegaly Generally Occurs via Five Mechanisms:

1. Inflammation
2. Excessive storage
3. Infiltration
4. Congestion
5. Obstruction [2]

Early diagnosis and treatment of children who have liver disease is important because specific treatments are available for some diseases that can prevent disease progression or hepatic failure.

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As many number of pathological conditions and few secondary to cardiac conditions,pulmonary conditions are also often being seen associated with hepatomegaly the study is relevant to existing situation.

Materials and Methods

Hundred consecutive cases, from birth to 18 years of age with varying grades of hepatomegaly of different etiologies, admitted in pediatric wards of NMCH&RC were studied from Jan2015 to Dec2015.

On admission, detailed study of each case including history, through physical examination and necessary investigations within the limitations of available laboratory facilities were done depending upon the history and clinical findings.

The examination of cases was done according to the given proforma. Enlargement of the liver less than 4cm below right subcostal margin was graded as mild, between 4-7 cm or upto the umbilicus is graded as moderate and more than 7cm or beyond the umbilicus as massive [3].

Routine investigations like complete blood count, peripheral smear, urine, and stool analysis, chest x-ray, mantoux test were done initially.

Relevant investigations like WIDAL, HIV, HbSAG, HAV, LFT, Bone marrow examination, bleeding time, clotting time, Hb electrophoresis, Liver biopsy,blood group, blood culture was done in relevant cases, depending upon the provisional diagnosis made on history and clinical examination.

Observation and Results

Sex Distribution

Table 1: Shows sex incidence

Sex	No. of Cases
Male	62
Female	38

Age Distribution

Table 2: Shows the age distribution

Age in years	No. of Cases	Percentage
< 1year	16	16
1-4	34	34
5-8	29	29
9-12	12	12
13-18	09	09

Table 3: Shows Symptoms and Signs Associated with hepatomegaly:

Sl. No.	Symptoms	Percentage
1	Fever	73
2	Facial puffiness/edema of feet	19
3	Jaundice	37
4	Breathlessness/Hurried breathing	11
5	Pain in abdomen	10
6	Distension of abdomen	09
7	Vomiting	26
8	Mass in abdomen	08
9	Failure to thrive	04
10	Neonatal Jaundice	03
11	Altered level of conciousness	06
12	Convulsions	04
	SIGNS	
13	Spleenomegaly	78
14	Anemia	48
15	Lymphadenopathy	52

Table 4: Shows grades of hepatomegaly

Grades of hepatomegaly	Percentage
Mild(below 4cms)	64
Moderate 4-7cms	32
Massive >7cms	04

Table 5: Shows etiological groups of 100 cases

Etiological Analysis	Percentage
Infectious	48%
Heamatologic	12%
Miscellaneous	14%
Congestive	18%
Malignancy	04%
Cholestatic	03%
Metabolic	01%

Table 6: Shows etiological analysis of 100 cases

Infections	
A. Acute	48
Infective Hepatitis	18
Enteric fever	09
Malaria	08
Dengue	04
Pyogenic meningitis	02
Infective endocarditis	01
B. Chronic	
Tuberculosis	04
Chronic hepatitis	02
HIV	02
Hematological :	
Thalassemia	08
Sickle cell disease	03
Heriditary spherocytosis	01
Miscellaneous:	**14**
PEM	08
Rheumatic fever	04
Juvenile rheumatoid arthritis	02
Malignancy	**04**
Leukemia	02
Lymphoma	01
Neuroblastoma	01
Congestive	**18**
CHD	14
Constrictive pericarditis	03
Budd-chiari syndrome	01
Cholestatic	**03**
Biliary atresia	02
Gall stones	01
Metabollic	**01**
Glycogen storage disease	01
Hematological :	
Thalassemia	08
Sickle cell disease	03
Heriditary spherocytosis	01
Miscellaneous:	**14**
PEM	08
Rheumatic fever	04
Juvenile rheumatoid arthritis	02
Malignancy	**04**
Leukemia	02
Lymphoma	01
Neuroblastoma	01

Congestive	**18**
CHD	14
Constrictive pericarditis	03
Budd-chiari syndrome	01
Cholestatic	**03**
Biliary atresia	02
Gall stones	01
Metabollic	**01**
Glycogen storage disease	01

Table 7: Shows age incidence in each etiological group

Age	Infection	Hematologic	Congestive	Malignancy	Cholestasis	Miscellaneous	Storage
<1yr	01	04	08	00	02	01	0
1-4y	14	06	05	02	01	05	01
5-8y	19	02	03	01	0	04	0
9-12	07	00	02	01	0	02	-
13-18	07	00	-	-	-	02	-

Table 8: Shows incidence of each grade of splenomegaly in each etiological group

Grades of hepatomegaly	Infections	Hematological	Miscellaneous	Congestive	Malignancy	Storage Disorders	Cholestasis
Mild(2-4) cms	37	06	10	10	00	00	01
Moderate(4-7)cm	11	05	04	07	02	01	02
Massive >7cm	00	01	00	01	02	00	00
Total	48	12	14	18	04	01	03

Table 9: Shows analysis of consistency of 100 cases

Consistency	Percentage
Soft	88
Firm	12

Discussion

Age Incidence

In this study 100 cases were studied with ages ranging from birth to 18 years of age. 16% of cases belonged to the age group of birth to 1year, 34% from one to 4 years, 29% from 5 to 9 years of age, 12% from 9to12 years of age and 9% from 13-18 years of age. The data suggests that incidence of hepatomegaly is higher in children below 9 years of age. It may be due to common occurrences of infections in this age group like viral hepatitis.

Sex Incidence

Males were affected more than females. In our study 62% of the affected children were males and 38% were female. Studies on various diseases which cause hepatomegaly like dengue fever,visceral leishmaniasis, chronic myeloid leukaemia also show male preponderance [4,5,6].

Presenting Symptoms

Children in our study presented with various symptoms depending upon the etiology some symptoms were specific whereas others were vague.

1. *Fever:* Fever was the most common presenting symptom seen in 67% of children of our study. It was seen in infections, infestations and malignancies.
2. *Vomiting:* Vomiting is seen in 26% of the cases was associated with various infections like TB meningitis due to raised ICT, in enteric fever, in viral fever associated with gastritis and mechanical discomfort as in ascites.
3. *Jaundice:* Jaundice was the presenting symptom in 37% of cases and was associated with cirrhosis of liver, infective hepatitis, typhoid due to hepatocellular dysfunction,It was seen in haemolytic anemias due to degradation of abnormal haemoglobin.
4. *Swelling of the face or feet*: Swelling of the face or feet was seen in 19% of cases and associated with severe anemias, PEM and congestive cardiac failure.
5. *Breathlessness:* Breathlessness/hurried breathing was seen in 11% of cases was due to associated

lung infections or congestive heart failure.

6. *Pain in abdomen:* Pain in abdomen was associated with 10% of cases due to tumours and acute hepatitis.
7. *Distension of abdomen*: Distension of abdomen was seen in 9% of cases may be due to organomegaly or free fluid like ascites.

Signs

The commonest sign associated with hepatomegaly was splenomegaly followed by anemia and lymphadenopathy.

1. *Splenomegaly:* Splenomegaly was seen in 78% of cases was associated with infections, haemolytic anemias, leukemias and congestive disorders.
2. *Anemia:* Anemia seen in 48% of cases was associated with haematological disorders, malignancy, congestive disorders and storage diseases.
3. *Lymphadenopathy:* Lymphadenopathy seen in 52% of cases was associated with leukemias, HIV, viral fever, enteric fever.

In a study from Brazil fever,pallor,weight loss and jaundice were the most common presenting symptoms [6]. Most studies show that fever is the most common presenting symptom associated with hepatomegaly [6,7,8]. A study on hepatosplenomegaly and anemia also observed that fever was the most common presenting symptom followed by abdominal distension, pallor, failure to thrive, oedema, dyspnea and jaundice [9].

Etiological Analysis of Hepatomegaly

1. *Infections Group:* In the present study, 48% of cases shows infectious etiology forming the most common cause of hepatomegaly in children.Out of those 48% cases 40% are acute infections and other 8% are chronic infections.

Among the 48% of acute infections group infective hepatitis 18%, enteric fever 9%, malaria 8%, dengue 4%, pyogenic meningitis 2%, infective endocarditis 1%. Among the 8% cases of chronic infectious group tuberculosis 4%, chronic hepatitis 2%, HIV 2%.

According to WHO infectious diseases accounted for 41.5% of total global DALY(Disability Adjusted Life Years). Communicable diseases like malaria, tuberculosis, HIV are highly prevalent.A study done in 2011 in Guntur shows infectious group as the most common cause of hepatomegaly in children.In a study done in Uttaranchal shows infectious group as the most common cause of hepatomegaly in children [10].

2. *Congestive Group*: It comprised of 18% of cases in our study out of which 14% were due to congenital heart diseases, 3 were due to acquired constrictive pericarditis, and 1% due to buddchiarisyndrome. As compared to a similar study done in Guntur congestive causes in our study are low [10].
3. *Hematological causes*: This constituted 12% cases in our study.Out of which 8 were thalassemia major, 2 were sickle cell disease and one was hereditary spherocytosis.

A study from Mumbai,on hepatosplenomegaly with anemia found thalassemia major as most common hemoglobinopathy on HB electrophoresis [9].

4. *Miscellaneous*: 14% of cases belonged to miscellaneous group. Out of which 8 were due to PEM, 4 were due to rheumatic fever, 2 were due to juvenile rheumatoid arthritis.
5. *Malignancy*: 4 cases belonged to malignancy group out of which 2 were due to acute lymphoid leukemia, one was due to lymphoma, and the other neuroblastoma.
6. *Cholestatic*: 3 cases were due to cholestasis out of which 2 were due to biliary atresia,and one was due to gall stones.
7. *Storage disorders:* Storage disorders comprised of only 1% in our study.

Analysis by Consistency

In our study consistency was evaluated based on palpation, 88% of livers are soft in consistency which is because of infections as predominant etiology, 12% are firm in consistency.

Analysis by Area

In our study majority of the are from rural areas 72% compared to urban as most of the cases admitted in our wards are from rural background and infection susceptibility is more in lower socio economic status.

Etiological Analysis of 100 Cases

Among the 9 cases of enteric fever only 3 had blood culture positive reports, others were diagnosed based on history, clinicalexamination, and positive WIDAL test. There were 8 cases of malaria 5 had positive peripheral smear for pl.falciparvum, 2 were positive for pl.vivax, 1 had mixed pl.falciparvum and vivax. 18 cases were due to infective hepatitis Hepatitis A virus (HAV) positive in 7 cases, IgM positive in 4

cases and 1 case having HbsAgpositive.One case had infective endocarditis, and had positive blood culture reports. Two cases had pyogenic meningitis which was confirmed by CSF study, 4 cases had dengue fever which was confirmed by dengue IgG and IgM, NS1Ag. Ten cases had chronic infections out of which 2 were positive for HIV, all were confirmed by positive HIV elisatest. Both of them had lymphadenopathy with diarrhoea and pyoderma.Four cases had tuberculosis out of which two had abdominal tuberculosis confirmed by ascitictap,and two had pulmonary tuberculosis.

In a study done on typhoid fever, 71 children presented with fever and gastro intestinal symptoms including abdominal pain, diarrhea, nausea, vomiting and constipation. Hepatosplenomegaly was most common physical sign followed by abdominal tenderness [46]. Another study on HIV from Mumbai showed that hepatosplenomegaly lymphadenopathy and opportunistic infections together in a child may suggest of HIV infection [49].

Fever, sweating, and hepatomegaly were common clinical findings in children with brucellosis [50]. Hepatomegaly was in 72% of cases in dengue fever [43]. In a study from central India, 70% of fever cases had malaria, out of which, 87%, were caused by pl. falciparvum [51].

Hematological Disorders

These constituted 12% of patients of our study, 8 were thalassemia major, 3 were sickle cell disease, one due to hereditary spherocytosis.

Hemoglobin levels ranged from 3 to 12.2gms/dl. Heamoglobinlevels, retic count and peripheral smear gave clue to diagnosis in many cases. Hemolytic diseases like thalassemia, were confirmed by Hb electrophoresis. 50 cases with hepatosplenomegaly with anemia were studied in Mumbai Hb electrophoresis showed 10 out of 12 cases with abnormal electrophoresis pattern, whereas one each had sickle cell anemia and Hbs/â thalassemia.The presenting features were fever followed by abdominal distension, failure to thrive, oedema, dyspnoea, jaundice. Hepatosplenomegaly and pallor were the main clinical signs [9].

Miscellaneous

14% belonged to the miscellaneous group. Out of which 8 were due to PEM, 4 were due to rhematic fever, 2 were due to juvenile rheumatoid arthritis.

Two cases were juvenile rheumatoid arthritis diagnosed by positive RA factor. Eight cases were PEM diagnosed by clinical features and examination. 4 cases of rheumatic fever diagnosed after fulfilling modified jones criteria.

Congestive Group

18% belonged to the congestive group out of which 14 were of CHD 6 had VSD, 3 had PDA, 3 had TGA, one had trisuspid atresia and one had ebsteinsanomaly. They were diagnosed by chest x-ray, 2-D Echo and clinical findings. Y. Shivaramakrishna study showed 32% belonged to congestive group [10].

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Malignancy

4 cases belonged to malignancy group,out of which 2 were acute myeloid leukemia,one was acute lymphoblastic leukemia and one was neuroblastoma. The cases were confirmed by bone marrow by bone marrow examination. All cases of malignancy had significant lymphadenopathy. In a study in 530 patients with acute lymphoblastic leukemia from India, the authors found that the most common features were lymphadenopathy and hepatos plenomegaly [11].

Cholestatic

3 cases belonged to cholestatic group out of which 2 were due to biliary atresia diagnosed by triangular cord seen on USG and one was due to gall stones diagnosed by x-ray and USG.

Storage Disorders

One case belonged to storage disorder and it is Glycogen storage disease diagnosed by clinical features and liver biopsy.

Conclusions

- Maximum incidence of hepatomegaly was seen in 1-4 years age group and with Male preponderance.

- Mild hepatomegaly (2-4cm) was the most common grade of hepatomegaly Commonest causes were infectious causes.
- Fever was the most common presenting feature in our study associated with hepatomegaly.
- Among infections, infective hepatitis 18% is the most common cause followed by enteric fever 9%.

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Original Article

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Treatment Pattern in Children with Lower Respiratory Tract Infection in a Tertiary Care Hospital of Eastern India

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Abstract

Lower respiratory tract infections (LRTIs) are the leading cause of death among infectious diseases and responsible for large burden of avoidable morbidity and mortality in childhood. The present study was done to assess the prescribing pattern of drugs in LRTI in children aged 1 month-14 years old using WHO core antibiotics drug prescribing indicators. This was a cross sectional, record based study carried out for a period of 1 year in the Department of Pharmacology in collaboration with Department of Pediatrics, PBMH, KIMS, Bhubaneswar. This study was approved by KIMS research committee and institutional ethics committee. Study states that LRTI (42%) was highest in the incidence followed by WALRI. Most commonly prescribed antibiotic was Cephalosporin group (Ceftiraxone) followed by Amikacin. Levosalbutamol with Ipratropium was the most commonly used nebulizing drug followed by combination with steroid (budesonide). Antibiotics were prescribed for 245(100%) patients followed by bronchodilators, antipyretics, cough medications, oxygen inhalation, nasal decongestants, steroids and others which include multivitamins. Admissions of males (70.6%) were more as compared to females(29.4%) indicating gender bias is still persisting in society. Antibiotics stewardship is very much needed to prevent its overuse and emergence of resistances.

Keywords: Hospital Stay; Prescription Pattern; Antibiotics; LRTI.

Introduction

LRTI is infection below the level of larynx and used synonym for Pneumonia, can also be applied to others type of infection including bronchiolitis, bronchitis, lung abscess and laryngotracheobronchitis [1]. LRTI is one of the most common conditions encountered in Pediatric Departments during the winter months and its management consumes substantial health-care resources [2]. As reported in 2015, 3.6million (3.3-3.9million) episodes of severe pneumonia and 0.35million (0.31-0.40million) of all causes of pneumonia deaths occurred in children younger than 5years in India [3]. According to global burden of disease study estimated that LRTI include CAP (Community Acquired Pneumonia), were 492.2 million episodes of illness worldwide and accounts for 49.5million disability adjusted life years (DALYS). In children aged over 5years, it causes 1.6million deaths annually [4]. Worldwide, infants and children represent a higher proportion of the population. 28% of the world's total population is accounted by children younger than 15 years of age. In developing countries 25% of all pediatric admissions are due to acute respiratory tract infections and which ultimately causes death of 3.5 million children each year [5]. Pediatric population is prone to suffer from recurrent infections of the respiratory tract [6]. The use of antimicrobial agents, especially antibiotics has

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become a routine practice for the treatment of pediatric illness [7]. Essential drugs offer a cost-effective solution to many health problems in a developing country [8].

Objectives

To study the following parameters in the study population-

- Sociodemographic profile of the subjects diagnosed with LRTI.
- Prescriptions for LRTI for pattern of antibiotics use and alterations of antibiotics.
- Assess the subject for possible associations between living conditions and the disease or course of disease.

Materials and Methods

Study Type and Duration

This was a cross sectional observational, record based study carried out for a period of 1 year (Aug 2016 to July 2017) in the Department of Pharmacology in collaboration with Department of Pediatrics, PBMH, KIMS, Bhubaneswar. This study was approved by KIMS research committee and institutional ethics committee. A total of 245 inpatients fulfilling the inclusion criteria were included. Current diagnosis, treatment chart, length of hospital stay, empirical and combinations of antibiotics on admission to discharge were recorded and analyzed.

Inclusion Criteria

- Pediatric patients admitted within the age group of (1mo-14 years) diagnosed with LRTI.

Exclusion Criteria

- Patients having chronic diseases (cystic fibrosis, on long standing steroids, failure to thrive, immunodeficiency, any coexisting infections (urinary or meningeal)
- OPD patients.
- Left against Medical advice during the course of treatment.

Data Collection

Data was collected from total of 245 pediatric in-patients treated for Lower respiratory tract infection (Bronchiolitis, Bronchitis, Laryngotracheobronchitis, wheeze associated with LRTI) aged between (1mo-14yrs) fulfilling the inclusion criteria were taken. Demographic profile, antibiotics prescribed, use of oxygen, other drugs used are collected. A written informed consent was obtained from parents/ guardians of all the children after explaining the study procedure.

Statistical Analysis

Collected Data was be analyzed using GRAPH-PAD statically software to find any statically significant difference. Categorical data were expressed as percentage and average as comparative statistical analysis. Necessary statistical figures were shown using Bar Diagram, Chart and other necessary tools.

Results

The number of children diagnosed with lower respiratory tract infection is maximum in the age group of 0-1 yrs and accounts for 49.8% of total children admitted with LRTI. There is a fall in the number of children admitted with LRTI beyond 1 year age to almost $1/4^{th}$ of this value with a small surge of cases in the age group of 6-10 years. Overall there is strong significant association between age of patients and the types of disease ($p<0.001$).

Table 1: Distribution of Disease in Male and Female

Types of Disease	Sex		Total
	Female	Male	
Bronchiolitis	11	31	42
Lrti	38	64	102
Pneumonia	9	44	53
Walr	14	34	48
Total	72	173	245

As p-value<0.05 there is significant relationship between sex and types of disease

Table 2: Disease Distribution in different Age group

Types of Disease	Age				Total
	0-1 years	2- 5 years	6- 10 years	11- 14 years	
Bronchiolitis	34	3	3	2	42
Lrti	40	16	31	15	102
Pneumonia	10	6	24	13	53
Walr	38	8	1	1	48
Total	122	33	59	31	245

Different types of diseases with different age group of admitted children and their incidence.

Fig. 1:

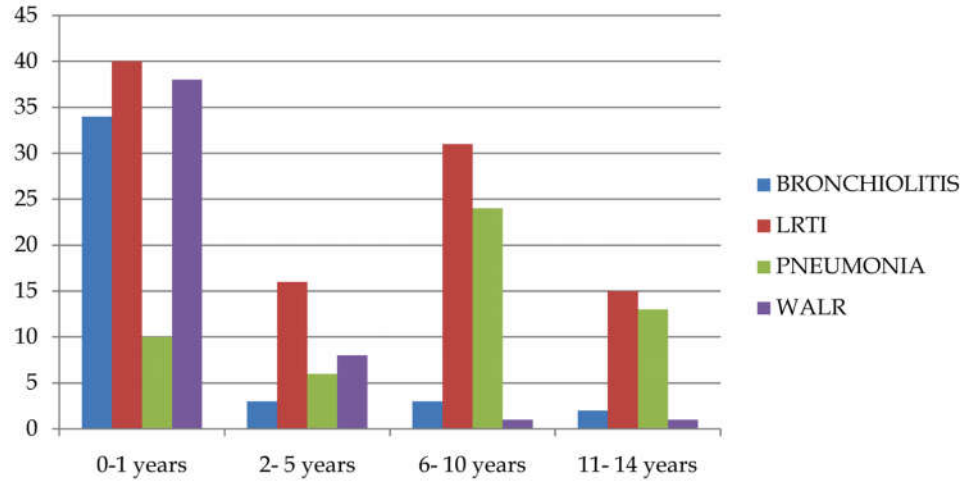

Table 3: Empirical Antibiotics Used in Male and Female Gender Distribution

Antibiotics Used	Sex		Total	Chi-square/Exact test	DF	P-value
	Female	Male				
AMIKACIN	5	16	21	6.956	9	0.642(*)
AMIKACIN,AMP	2	2	4			
AMIKACIN,PIP	0	1	1			
AMOXICILLIN	1	9	10			
AMPICILLIN	0	4	4			
AMPICILLIN,CLOXACILLIN	1	4	5			
AZITHROMYCI	1	1	2			
CEFTIRAXONE	62	134	196			
CIPROFLOXAC	0	1	1			
PIPERACILLI	0	1	1			
Total	72	173	245			

Fig. 2:

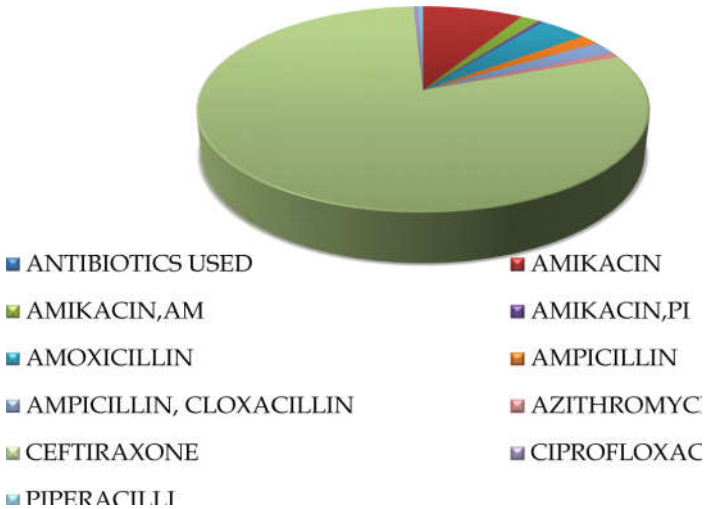

Fig. 3:

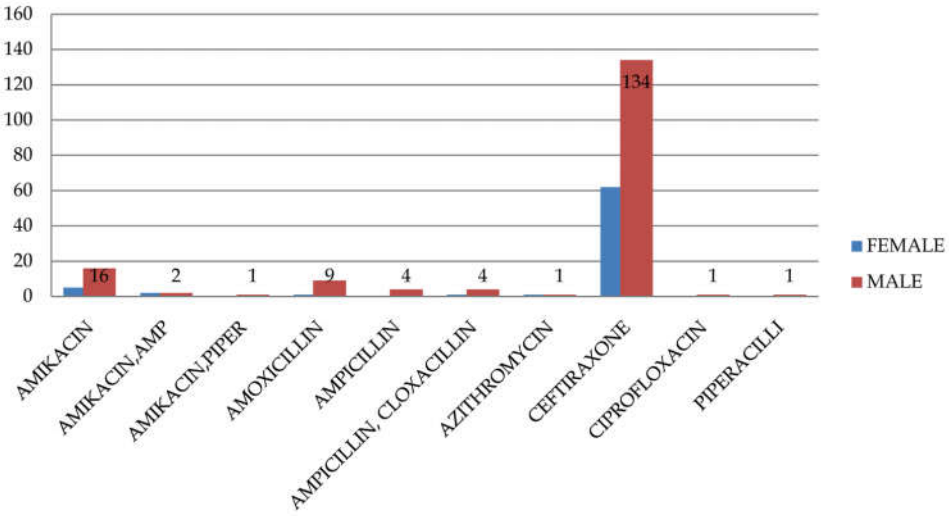

Table 4: Empirical Antibiotics Used in different Age group

Antibiotics Used	Age				Total	Chi-square	DF	P-value
	0-1 years	2- 5 years	6- 10 years	11- 14 years				
AMIKACIN	8	6	4	3	21	33.44	27	0.183(#)
AMIKACIN,AMP	3	0	1	0	4			
AMIKACIN,PIP	0	1	0	0	1			
AMOXICILLIN	6	1	2	1	10			
AMPICILLIN	4	0	0	0	4			
AMPICILLIN, CLOXACILLIN	5	0	0	0	5			
AZITHROMYCI	1	0	0	1	2			
CEFTIRAXONE	94	25	52	25	196			
CIPROFLOXAC	0	0	0	1	1			
PIPERACILLI	1	0	0	0	1			
Total	122	33	59	31	245			

Table 5: Nebulizer drug used in Male and Female Gender Distribution

Nebulizer Drug Used	Sex		Total	Chi-square	DF	P-value
	Female	Male				
Levosalbutamol	20	57	77	3.299	4	0.509($)
Levosalbutamol, Budesonide	3	11	14			
levosalbutamol, budesonide, hydr	12	26	38			
Levosalbutamol,Hydrocortis	9	11	20			
Levosalbutamol,Ipratropium	28	68	96			
Total	72	173	245			

As p-value>0.05 there is no significant relationship between antibiotics used and age (Table 3). Out of 245 patients studied, highest numbers of patients were infants with 122 patients having age less than 1 year there were less patients in the older age groups. However there was no antibiotic preference for any particular age group as p-value >0.05 for this correlation indicating that there is no significant relationship between antibiotics used and age.

Ceftriaxone was the most commonly used antibiotic administered to 196 patients followed by amikacin with 21 cases (Figure 1).

Asp-value>0.05 there is no significant relationship between age and nebulizer drug used (Table 4). In addition to antibiotics used all the patients were administered nebulization therapy. Levosalbutamol, ipratropium, budesonide, hydrocortisone were the drugs used in varying combination for nebulization purpose. However there is no significant relationship between age and nebulizer drug used with p value >0.05.

Table 6: Nebulizer drug used in different Age group

Nebulizer Drug Used	Age				Total	Chi-square	DF	P-value
	0-1 years	2- 5 years	6- 10 years	11- 14 years				
Levosalbutamol	40	10	15	12	77	14.232	12	0.286(**)
Levosalbutamol,Budesonide	12	0	2	0	14			
Levosalbutamol,Budesonide, Hydr	14	7	10	7	38			
Levosalbutamol,Hydrocortis	8	3	7	2	20			
Levosalbutamol,Ipratropium	48	13	25	10	96			
Total	122	33	59	31	245			

Discussion

In general practice, the therapeutic approach for lower respiratory tract infection is primarily empirical and the main aim of the physicians is to treat as specifically as possible. The present study indicates the general trends of use of antibiotics in lower respiratory tract infection in pediatric inpatient department. Antibiotic resistance is an emerging problem and has become a major threat to the medical field. Excessive and in appropriate use of antibiotic has been a major contributor to this ever growing problem.

Age Distribution

The total population was categorized into four groups and patient in each group were recorded. The data from our study represent that, out of 245 patients the highest number of patients in age group 0-1yr (113; 46.12%), 1-5yr (36; 14.69%), 6-10yr (74; 30.20%) and 11-14yr (22; 8.97%). i.e. highest number of patients were in age group 0-1yr and lowest number were in age group 11-14yr. So the mean age of pediatric patient was 51.608 (in months) or 4.30 (in years).

Among all pediatric patients 101 patients (41.22%) were diagnosed with LRTI, 67 patients (27.34%) with Pneumonia, 46 patients (18.77%) with WALRTI, 28 patients (11.48%) with Bronchiolitis, 2 patients (0.81%) with Bronchitis, and 1 patient (0.40%) with Laryngotracheobronchitis. The highest numbers of patients were diagnosed with LRTI and lowest numbers of patients were diagnosed with Laryngotracheobronchitis.

Other studies of children with LRTI shows the highest number of patients were in age group less than a year i.e. 38.1% and lowest number were in age group 9-11 i.e. 0.6% [9]. It was seen that patients from age group 2-14yrs were 42.27%, followed by <12months were 32.73% with LRTIs [10]. In our study the mean age of pediatric patient affected with LRTI was 4.3 years.

Most of the hospitalized pediatric patients belonged to age group of less than one year. This is indicative of susceptibility of infant below one year towards various infective diseases. It was revealed that infant less than one year received antibiotics more frequently than older children. The author also stated that this could be due to higher susceptibility of infections at a younger age and needs a greater concern for infant's health relatively [11]. But if we take admission to pediatrics ward, patients being hospitalized belongs to age group 5-12yr [7].

Types of diseases in different age is statistically significant as 0-1yr age group was having higher occurrence of subtypes of LRTI except pneumonia which is more in 6-10 years of age group.

Disease Diagnosed

Among all 245 pediatric patients 101 patients (41.22%) were diagnosed with LRTI, 67 patients (27.34%) with Pneumonia, 46 patients (18.77%) with WALRTI, 28 patients (11.48%) with Bronchiolitis, 2 patients (0.81%) with Bronchitis, 1 patient (0.40%) with Laryngotracheobronchitis. The highest numbers of patients were diagnosed with LRTI and lowest numbers of patients were diagnosed with Laryngotracheobronchitis.

Another study shows 55.46% patients were diagnosed with Bronchopneumonia being highest in the incidence followed by WALRI and Bronchiolitis [10]. Few studies, states that WALRI is the highest incident followed by Broncho-pneumonia [5]. In a report prepared by International Vaccine Access Center (IVAC) in 2014 revealed that Pneumonia in developing countries remains fairly stagnant despite of major reductions in globally.

Most of authors state that Pneumonia is still a leading killer of young children through there are simple, safe, effective and expensive interventions to minimize the risk. They also emphasized that the reason could be poverty and lack of access to healthcare in developing countries [15].

Number of Antibiotics Per Prescription

Third generation, ceftriaxone (80%) was the leading antibiotic prescribed followed by amikacin (9%), amoxicillin (4%) and ampicillin (1.6%). The least prescribed antibiotics were cloxacillin, azithromycin and piperacillin. Higher prescription rate of cephalosporin could be attributed to its broad spectrum of activity and tolerance across all age group.

Study revealed that 127 (51.83%) patients were on monotherapy of antibiotics followed by 73 (29.79%) patients were on two combination antibiotics therapy, 41 (16.73%) patients were on three combination antibiotics therapy and 4 (1.63%) patients were receiving more than three combination antibiotics therapy. So the mean average number of antibiotics per prescription of patient staying in hospital ward was 1.68.

A studies comprising of 150 case records of children, most patients were put only one combination of antibiotic (45.3%) and others were put on two antibiotics (33.3%) which is a very good clinical practice observed [9]. Average number of drug is an important indicator for assessing rationality of prescription. It is preferable to keep the mean number of drugs per prescription as low. The WHO recommends that the average number of drugs per prescription should be less than 2 [13]. The average number of drugs per prescription value should be as low as possible to prevent the unfavorable outcomes of polypharmacy such as increased risk of drug interactions, increased cost of therapy, non-compliance and emergence of resistance in case of use of antimicrobials [14].

Nebulized Drugs Used

According to our study the different bronchodilators used with steroids are levosalbutamol with ipratropium 93 (37.95%), levosalbutamol 77 (31.42%), levosalbutamol followed with budesonide & hydrocortisone 39 (15.91%), levosalbutamol & hydrocortisone 21 (8.57%), levosalbutamol & budesonide 15 (6.12%). A study of 150 case records of children with LRTI analyzed, bronchodilators were observed in 90% of case records and Salbutamol (88.67%) was most commonly prescribed followed by Budesonide (70%) [9]. The American Academy of Pediatrics recommends that inhaled bronchodilators should not be used routinely for the management of Bronchiolitis. One possible exception is for LRTI with underlying reactive-airway disease and where wheeze is the hallmark symptoms of LRTI, short acting beta 2 agonists may be effective for individual patients. Intravenous Hydrocortisone was prescribed for 18% of patients in our study in addition to inhalational Budesonide but a meta-analysis of studies comparing systemic glucocorticoid treatment to placebo did not find any difference in the length of hospital stay or clinical score of infants and young children with LRTI from either group. Hence routine use of corticosteroids is not recommended according to standard treatment guidelines [15].

Conclusion

Rational use of drugs was largely influenced by knowledge and attitude and its importance had to be emphasized. This study included in medical education to have long term beneficial effects. Strict antibiotic prescribing policy may significantly overcome the overuse of antibiotics and reduce the development of resistance to antibiotics. This study will help the clinicians to know about pattern of Antibiotics used and types of LRTI in Pediatric patient.

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Review Article

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Hexavalent Vaccine

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Abstract

Combination vaccines that include multiple antigens in one vaccine are now a widely accepted as an effective means of eliciting protection against several disease at the same time. Owing to improvement in quality and convenient mode of administration, they have become part of routine paediatric practice. Hexavalent vaccine includes diptheria, tetanus, pertussis, hepatitis B, polio and Haemophilus influenzae type b antigens. The studies until now have shown that the vaccine is highly immunogenic and well tolerated. It is now a part of various primary and booster vaccination schedule as well as it is safely given with other vaccines.

Keyword: Hexavalent; Hemophilus Influenzae; Hepatitis B.; Pertussis.

Introduction

The introduction of injectable vaccines targeting new diseases into childhood immunization programs has resulted in the need for combination vaccines to reduce the number of injections given during early childhood. In India and other similar countries, the successful implementation of IPV depends on many aspects of vaccine delivery, including the availability of an effective and affordable vaccine. Combination (multivalent) vaccines have the potential to simplify the currently complex childhood immunization schedules, improve caregiver compliance, and reduce healthcare costs [1].

Hexavalent vaccines containing Diphtheria (D), Tetanus (T), Pertussis (P), Hepatitis B (HBV), Haemophilus influenza B (Hib) and the three IPV antigens have been considered logically and scientifically sound charioteers of such a strategy, and have been touted to be the ultimate combination vaccine for routine immunization. The use of combined vaccine which include several antigen in a single administration, have a number of potential benefits including a reduction in the number of visits and complication related to multiple intramuscular injection, decreased costs of stocking and administering separate vaccine and reduced risk of delayed or missed vaccination [2].

The development of new hexavalent combination vaccines targeting established pathogens is likely to assist in improving compliance and timelines of vaccination in infants.These formulation will however need to be monitored for medium and long term effectiveness amidst growing concern of waning immunity against disease such as pertussis when using acellular pertussis vaccine and possibly hep B. When using combination vaccine the vaccine works by causing the body to produce it's own protection against the bacteria and viruses that causes these different infections-

- Diphtheria
- Tetanus
- Pertussis
- Hep B
- Poliomyelitis
- Haemophilus influenzae type B [3]

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Content

After shaking the normal appearance of the vaccine is a whitish cloudy suspension it contains:

- Each 0.5 ml dose contains
- At least 20 IU of diphtheria toxoid
- At least 40 IU of tetanus toxoid
- 25 microgm of pertussis toxoid and
- 25 microgm of pertussis filamentous hemagglutinin
- 10 microgm of hep B surface antigen
- 40 D antigen units of polio virus type 1
- 8 D antigen units of polio virus type 2
- 32 D antigen units of polio virus type 3
- 12 microgm of haemophilus type B
- Polysaccharides conjugated to 23-36 microgm of tetanus protein
- The other ingredients includes Sodium phosphate dibasic

Potassium phosphate monobasic Trometamol, sucrose, essential amino acids (cysteine, tyrosine, arginine hydrochloride, Histidine, isoleucine, leucine, lysine hydrochloride, methionine, phenylalanine, threonine, tryptophan and valine) and water for injectionsn[4].

Available Vaccines

Hexavac® (Sanofi Pasteur MSD, Lyon, France) was licensed in Europe in October 2000 as a paediatric primary and booster immunization and is widely used in many European countries. One single dose is composed of D toxoid (≥20 IU), T toxoid (≥ 40 IU), pertussis toxoid (PT) (25 μg), pertussis filamentous haemagglutinin (FHA) (25 μg), HBsAg (produced from recombinant strain of the yeast *Saccharromyces cerevisiae*) (5.0 μg), P1 (Mahoney strain) (40 DAU), P2 (MEF 1 strain) (8 DAU), P3 (Saukett strain) (32 DAU) and Hib (polyribosylribitol phosphate) 12 μg conjugated to tetanus toxoid (24 μg). Several comparative, controlled clinical trials deemed Hexavac to be very effective in assuring long-term protection against all of the indicated target diseases with a high degree of safety and tolerance. It was also deemed non-inferior or equivalent to comparator vaccines, including both separate vaccine components and Infanrix hexa, the second hexavalent vaccine available in this time period. However, in September 2005 the European Medicines Agency recommended suspension of Hexavac marketing authorization because of the reduced immunization properties of the hepatitis B virus (HBV) component [5].

Infarix: ensed as Hexavac in 2000, Infanrix® (GSK, Riixensart, Belgium) hexa is the only hexavalent vaccine authorized for paediatric use in Europe. Its composition is similar to that of Hexavac with two main exceptions. In addition to the pertussis antigens PT and FHA, pertactin (PRN 8 μg) is also included. HBsAg is present in a doubled amount, 10 μg instead of 5 μg. Additionally, unlike Hexavac, Hib antigen needs to be reconstituted before use. Several studies have evaluated the immunogenicity, safety and tolerability of this vaccine after primary immunization (two or three doses in the first 6 months of age according to the schedules recommended for infants) and after a booster dose at 12–15 months of age in comparison with several DTaP-based pentavalent vaccines administered in conjunction with monovalent HBV or Hib vaccines. Several studies have also compared Infanrix hexa with Hexavac. Evaluation of immunogenicity was performed on blood samples drawn 1 month after the last primary series dose and 1 month after the booster administration. Antibody concentrations against D and T toxoids of ≥ 0.1 IU/mL, HBsAg of ≥ 10 IU/L, polyribosylribitol phosphate polysaccharide (PRP) of ≥ 0.15 mg/mL and/or ≥ 1 mg/mL (markers of short-term and long-term protective immunity, respectively) and against P1, P2 and P3 antigens of ≥ 1 : 8 were considered the cut-off values to evaluate seroconversion and seroprotection rates. Moreover, because no generally accepted seroprotective antibody levels for pertussis antigens were established, vaccine seroresponse/seropositivity rates against PT, FHA and PRN were assessed and vaccine response was defined as the proportion of patients with post-vaccination antibody titres of ≥ 5 U/mL in initially seronegative infants and minimal maintenance of pre-vaccination antibody titres in infants who were seropositive before vaccination (i.e. titres ≥ 5 U/mL). Seropositivity rates were defined as the proportion of infants with antibody titres ≥ 5 U/mL. Throughout all of the studies evaluating an immune response it was demonstrated that all components of Infanrix hexa were highly immunogenic and equivalent or non-inferior to comparators [6].

The same pharmaceutical company that produced Hexavac has developed a new hexavalent vaccine, Hexyon® (Sanofi Pasteur MSD, Lyon, France). It has the same composition against D, T, P, polio and Hib, but differs in hepatitis B content. Instead of 5 μg HBsAg produced from recombinant strain 2150-2-3 of the yeast *Saccharromyces cerevisiae*, it includes 10 μg of HBsAg produced in the yeast *Hansenula polymorpha.* Hexyon has been evaluated in several clinical trials and is currently registered in markets outside Europe for the primary immunization of children from 6

weeks of age and for booster vaccination up to 24 months of age. It is a liquid vaccine that does not require reconstitution of any component before injection, facilitating administration and reducing the risk of medication error. The immunogenicity of Hexyon used for primary vaccination has been evaluated after three doses of the vaccine, according to the recommended immunization schedules of the countries in which the trials were conducted When Hexyon was evaluated before and after booster dose, it was administered at 15–18 months of age. In all primary series trials. Hexyon immunogenicity and safety were compared with standard doses of licensed vaccines. Quadrivalent, pentavalent and hexavalent vaccines were used as comparators, with the addition of monovalent vaccines lacking in the combined preparations. Antibody concentrations against D, T, PT, FHA, P1, P2, P3 and Hib were generally evaluated with the same criteria and methods previously described for Infanrix hexa with the exception of pertussis antigens, for which an four-fold or greater increase from baseline in antibody concentration was predefined as the surrogate measure of seroconversion. Immune response was systematically similar to that obtained with comparators [7].

Storage

Keep it in refrigerator, store at 2°C to 8°C under these recommended storage conditions the vaccine is stable for 36 months after the date of manufacture. It should not be frozen.

Do not use vaccine after the expiry date which is stated on the carton after expiry. Do not use vaccine if the packaging is torn or show sign of tampering.

Keep out of reach and sight of children.

Keep vaccine in the original pack until it is time for it to be given.

Medicine should not be disposed of via waste water or household waste [8].

Dosage and Schedule of Vaccination

Vaccine should be administered intramuscularly. The recommended injection sites are generally the antero lateral aspect of upper thigh in infants and toddlers and deltoid muscle in older children. Primary vaccination schedule consists of three doses of 0.5 ml (such as 6,10,14 weeks) to be administered at an interval of at least 4 weeks. All vaccination schedules including the expand program on immunization can be used whether or not a dose of hep B vaccine has been given at birth where a dose of hep B vaccine is given at birth. The hexavalent vaccine can be used for supplementary doses of hep B vaccine from the age of 6 weeks. If a second dose of hep B vaccine is required before this age monovalent hep B vaccine should be used [9].

Booster Vaccination

After primary vaccination (e.g. 6, 10, 14 weeks; 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) with Hexaxim, a booster dose of HepB and Hib must be administered during the second year of life and at least 6 months after the last priming dose. In addition, if the priming schedule used is 6, 10 and 14 weeks a booster dose of polio vaccine should be given. Hexaxim or any other vaccine containing HepB, Hib and, if necessary, polio antigens may be used to accomplish boosting of the immune responses to these antigens.Booster doses should be given in accordance with the official recommendations [10].

Side Effects

1. Very common

   Pain redness loss of appetite sleeping vomiting Crying irritability fever
2. Common

   Abnormal crying diarrhea injection site hardness
3. Uncommon

   Allergic reaction lump at injection site high fever
4. Rare

   Rash large reaction at injection site
5. Very rare

   Pale flappy and unresponsive serious allergic reaction convulsions [11]

Contraindication

History of several allergic reaction to any component of the vaccine or to any pertussis vaccine after previous administration of vaccine or a vaccine containing the same component constituents. Encephalopathy of unknown etiology within 7 days of administration of a previous dose of any vaccine containing pertussis antigens [12]. In these circumstances pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria tetanus hep B polio and hib vaccine. Children suffering from progressive neurological disorders, uncontrolled epilepsy and progressive encephalopathy vaccination must be postponed in case of moderate or severe febrile and or acute disease [13].

Seroconvertion

The research paper by Chhatwal, et al. [7] published in this edition of Indian Paediatrics evaluates the efficacy of one such vaccine that is already approved in many countries, and is being used in their national schedules. The authors demonstrate very good seroconversion for all components even without a control group, and show how it can be integrated into the current immunization schedules. Moreover, the fully liquid preparations of hexavalent vaccines have distinct advantages over those which require reconstitution. Average preparation time is found to be almost half for the fully-liquid vaccine compared the non-fully-liquid vaccine. In the same study, almost all health care personnel (97.6%) stated that they would prefer the use of the fully-liquid vaccine in their daily practice [14].

Current Status

There have been a few issues with the combination vaccines themselves in the past. Hexavac (Sanofi Pasteur MSD, Lyon, France), which was licensed in Europe in 2000 as a pediatric primary and booster immunization, was recommended for suspension of marketing authorization by European Medicines Agency in September 2005 because of the reduced immunization properties of the HBV component [15]. However, the newer vaccine from the same manufacturers – Hexyon or Hexaxim – has a higher HBsAg content and uses a different method for its production. This seems to have resulted in higher immunogenicity compared to hexavac [16]. A possible temporal association between first immunization with hexavac and the occurrence of sudden unexpected death was also suspected. This claim was strongly refuted on further investigation. The other widely used hexavalent vaccine Infanrixhexa (GSK, Riixensart, Belgium), which contains three pertussis antigens (PT, FHA and PRN), has been demonstrated to be immunogenic, effective, safe and well tolerated in children regardless of gestational age at birth, and not significantly different from the vaccines used as comparators. The immunogenicity seems superior to Hexavac for hepatitis B until 7–9 years of age [17]. Furthermore, vaccination with this DTaP-HBV-IPV/Hib in infancy induces sustained seroprotection and immune memory against HBV even in 12-13 year-old adolescents . The comparison of this vaccine between two schedules in Indian infants has also been recently published. With regards to the current study, the immunological response with co-administration of PCV7 and rotavirus vaccine was not studied. Also, the persistence of seroprotection, especially with pertussis (having two antigens), and the effect of administration of rotavirus has not been studied [18].

Conclusion

Hexavalent formulations are already a necessary component of the vaccination Schedule, and would be even more pertinent in the days ahead. Seroconversion or seroprotective titres of antibodies against all antigens were achieved in the majority of infants following a primary series of three doses administered at 1-2-month intervals from 2 months of age. Hexavalent vaccine also induced immunologic memory, as evidenced by the anamnestic response to booster vaccination at 12-18 months of age [19]. These responses were comparable with those seen following concomitant administration of Pentavac (DTaP-IPV//PRP-T) and monovalent hepatitis B vaccine (H-B-Vax II), and were also within the ranges observed for other relevant licensed vaccines. However, they would need to be monitored for long-term effectiveness in view of the growing concern of waning immunity against diseases such as pertussis when using acellular-pertussis vaccine, and possibly hepatitis B when using combination vaccine [20].

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Review Article

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Recent Advances and Consensus Based Management Options for Lupus Nephritis in Children

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Abstract

Pediatric lupus nephritis, though rare; has significant morbidity and mortality. Often it may get undiagnosed or get diagnosed late due to lack of awareness about its intricacies of management. Hereby an effort is made to compile the recent definitions and advances in management of pediatric lupus nephritis.

Keywords: Nephritis; Lupus; Renal Hypertension.

Introduction

Systemic lupus erythematosus (SLE) is autoimmune disorder with formation of autoantibodies and immune complexes, causing inflammation and potential damage to a various target organs like skin, kidney, musculoskeletal system, lungs, heart and central nervous system. Paediatric SLE is more severe than SLE in adults, requiring aggressive treatment. SLE is more common in girls (4:3 pre-puberty; 4:1 post-puberty) [1]. American College of Rheumatology (ACR) has given 11 criteria for the diagnosis of SLE and if ≥ 4 criteria are present, disease is said to be positive with 95% of sensitivity and 96% of specificity (Table 1) [2]. Systemic lupus international collaborating clinics (SLICC) revised and validated the ACR, SLE classification criteria in order to improve clinical relevance and gave new classification to diagnose SLE in 2012 (Table 2) [3] . Luis et al conducted a comparison study between the two classification with 2055 SLE patients and found the sensitivity of SLICC 2012 was higher than ACR 1997 (93.2% versus 85.6%; P < 0.0001) [4]. Of all the patients with SLE, 15-20% is diagnosed during childhood [5]. Median age of onset

Table 1: ACR Criteria for Classification of SLE* [2]

Malar rash
Discoid rash
Photosensitivity
Oral ulcers
Arthritis: non-erosive, affecting ≥2 joints
Serositis: Pleuritis, Pericarditis, peritonitis
Renal disorder: Proteinuria (≥ 0.5 g/day or persistently > +++), RBC casts
Neurological disorder: Seizures, Psychosis (exclude other causes)
Hematological disorder: Hemolytic anemia, Leukopenia (<4000/ mm^3 on two occasions), Lymphopenia (<1500/ mm^3 on two occasions), Thrombocytopenia (<100000/mm^3)
Immunological disorder: Elevated antinuclear antibodies (after exclusion of drug-induced lupus), anti–double stranded (ds) DNA and anti-Smith antibodies, Positive antiphospholipid antibodies
Antinuclear antibody positive

*Presence of 4/11 criteria establishes the diagnosis of SLE.

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of childhood SLE is between 11 and 12 years (rare below 5 years), and 80% of patients are female [6,7]. Renal disease in childhood SLE is present in up to 80% of Asians which is much higher than other part of world and is called Lupus Nephritis (LN) [8]. Glomerulonephritis is the most important cause of morbidity and mortality. LN usually arises within 5 year of diagnosis of SLE; however, renal failure rarely occurs. According to a study done in Madhya Pradesh from 2011 to 2015, LN was the commonest feature at disease onset, at the time of diagnosis and throughout the disease course among children with SLE [9].

Table 2: Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for Systemic Lupus [3]

Clinical Criteria	Immunological Criteria
Acute cutaneous lupus Malar rash, bullous lupus, toxic epidermal necrolysis variant of SLE, maculopapular lupus rash, photosensitive lupus rash or subacute cutaneous lupus	**Positive antinuclear antibody**
Chronic cutaneous lupus Classic discoid rash, lupus panniculitis, mucosal lupus, lupus erythematous tumidus, chilblains lupus, discoid lupus/lichen planus overlap	**Positive double-stranded DNA antibody**
Oral or nasal ulcers	**Positive anti-Smith antibody**
Nonscarring alopecia	**Antiphospholipid antibody positivity** Positive lupus anticoagulant, high titer anticardiolipin antibody (IgA, IgG, IgM), or positive anti–B2-glycoprotein I antibody (IgA, IgG, IgM)
Synovitis (≥2 joints)	**Low complement** Low C3, C4, or Ch50 level
Serositis Pleurisy or pericardial pain ≥1 day, pleural effusion or rub, pericardial effusion or rub, ECG evidence of pericarditis	**Positive direct Coombs test** (in the absence of hemolytic anemia)
Renal RBC casts + or urine protein/creatinine ratio >500 mg protein/d	
Neurologic Seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial neuropathy or acute confusional state	
Hemolytic anemia	
Leukopenia (<4,000/mm3) or **lymphopenia** (<1,000/mm3)	
Thrombocytopenia (<100,000/mm3)	

* Presence of 4 criteria (including at least 1 clinical and 1 immunologic criterion) establishes the diagnosis of SLE. These criteria were developed for classification in clinical trials and not for clinical diagnosis.

Prevalence and Incidence

The manifestation of SLE varies with racial, ethnic, environmental and genetic factors. Prevalence study data is sparse in India. According to one study of North India with population survey of 91,888, a point prevalence of SLE was 3.2 per 100,000 (95% CI = 0-6.86 per 100,000) [10]. This is a much lower figure than reported from the west. In a prospective epidemiologic study of 5.78 million Taiwan children of age less than 16 years, the prevalence of pediatric SLE was 6.3 per 100,000 (95% CI: 5.7-7.0) which was 6.2 more times more common in girls than boys. (11.2 per 100,000, 95% CI: 10.0-12.5 VS 1.8 per 100,000, 95% CI: 1.4-2.4) [6]. In Asia overall incidence rates for SLE ranges from 0.9 –3.1 per one lac population, while prevalence rates ranges from 4.3– 45.3 per one lac population [11]. Higher rates of renal involvement, one of the main systems involved at death, were observed for Asians (21– 65% at diagnosis and 40 – 82% over time) than for whites [11].

According to a metaanalysis published in 2010, Asians SLE patients are more prone to develop LN because of Fcã receptor IIIA-V/F158 polymorphism [12]. According to many studies the incidence of Lupus nephritis is higher in African, Asian and Latin American Mestizo populations compared to Caucasians [13,14,15,16]. Genes variation in different ethnics may be responsible for this variability.

Classification

The histological classification of lupus nephritis (LN) was initially proposed in 1975 by the World Health Organization (WHO) and modified in 1982 and 1995 (Table 3) [17].

Table 3: WHO Classification of lupus nephritis (1995) [17]

WHO class I : minimal mesangial LN	Light microscopy- no histological anormality Immunoflorescence/ electron microscopy – mesangial immune deposits.
WHO class II: Pure mesangial alterations	a. Mesangial widening and/or mild hypercellularity b. Moderate hypercellularity
WHO Class III nephritis Focal segmental glomerulonephritis	a. With active necrotizing lesions b. With active and sclerosing lesions c. With sclerosing lesions
WHO class IV Diffuse glomerulonephritis	a. Without segmental lesions b. With active necrotizing lesions c. With active and sclerosing lesions d. With sclerosing lesions
WHO class V nephritis: Diffuse membranous glomerulonephritis	a. Pure membranous glomerulonephritis b. Associated with lesions of class II c. Associated with lesions of class III d. Associated with lesions of class IV
WHO class VI nephritis:	Advanced sclerosing glomerulonephritis

Table 4: Classification of lupus nephritis (ISN/RPS) 2002 [18]

ISN/RPS Working Group - Revised Histopathological Classification of LN (Revised after a consensus conference in 2002)

1. Minimal mesangial LN – LM : Normal glomeruli
IF : Mesangial immune deposits

2. Mesangial proliferative LN –
LM : Purely mesangial hypercellularity of any degree or mesangial matrix expansion with mesangial immune deposits
IF or EM : none / few isolated subepithelial or subendothelial deposits

3. Focal LN - Active or inactive focal (<50% involved glomeruli), segmental, or global endo- or extra-capillary GN, typically with focal, subendothelial immune deposits, with or without focal or diffuse mesangial alterations.
III (A) Active focal proliferative LN
III (A/C) Active and sclerotic focal proliferative LN
III (C) Inactive sclerotic focal LN

4. Diffuse segmental (IV-S) or global (IV-G) LN - Active or inactive diffuse (>50% involved glomeruli), segmental, or global endo- or extra-capillary GN with diffuse subendothelial immune deposits, with or without mesangial alterations.
This class is divided into: **diffuse segmental (IV-S)** when >50% of the involved glomeruli have segmental lesions, **diffuse global (IV-G)** when >50% of the involved glomeruli have global lesions.
IV (A) : Active diffuse segmental or global proliferative LN
IV (A/C) : Diffuse segmental or global proliferative and sclerotic LN
IV (C) : Diffuse segmental or global sclerotic LN

5. Membranous LN - LM and IF or EM: Numerous global or segmental subepithelial immune deposits ± mesangial alterations. May occur in combination with III or IV in which case both will be diagnosed.

6. Advanced sclerotic LN: ≥90% glomeruli globally sclerosed without residual activity.

Transformation of the histologic lesion from one class to another is common especially in inadequately treated patients and usually results in progression to a more severe histologic lesion. WHO classification was modified in 2002 (Table 4), by International Society of Nephrology and Renal Pathology Society Working Group (ISN/RPS) [18]. The most striking advantage of ISN/RPS classification is the high interobserver and intraobserver reproducibility with clinical relevance and association resulting from a uniform reporting system used around the world [19,20].

According to a South Indian study, done from jan 1999 to dec 2004, diffuse proliferative glomerulonephritis (WHO Class- IV) was the commonest class, seen in 63% of cases whereas in Asia it was found in 39.4–54% of case of LN [21,22] .

In India, it was reported that the most common secondary glomerulonephritis was LN (80.1%) [23, 24]. Renal histopathology guides for the introduction of appropriate treatment.

Pathophysiology

Generation of autoantibodies directed against self-antigens causes damage to target organs like kidney, skin, musculoskeletal system, heart, lungs and CNS. Antibodies to ds-DNA form immune complexes, which deposit in glomeruli, and initiate inflammation leading to glomerulonephritis. In more severe forms

of LN, proliferation of endothelial, mesangial and epithelial cells occurs and the production of matrix proteins lead to fibrosis [25] Pathogenesis of LN which involves autoimmunity is a complex process which involves role of the complement cascade which opsonises the immune complex, autoantibodies, breaking of tolerance, immunity and innate immune system in driving renal damage. Interferon gamma, IL-17 and compensatory FOXP3 levels are elevated, which indicates role of Th1 and Th17 for determining severity of LN [26]. The innate immune system may induce the adaptive immune system through toll like receptors by activating auto-reactive B cells and instigating a T cell response [27].

Clinical Presentation

According to a Taiwan study done between January 1999 and December 2011, in pediatric SLE patients the mean age at diagnosis was 12.4±2.5 years (range, 4.0–17.2 years) and the female-to-male ratio was 5.94:1 [28]. Hormonal influence is the cause of female predominance. Increased estrogen, prolactin and decreased androgen at pubertal age were considered the cause of this predisposition, which was proved in mouse models. But in human, little evidence was found with estrogen and prolactin related exposure. In a study done at south west Asia, Oman most common clinical features were articular (76%), followed by mucocutaneous (70%), haematological manifestations (68%) and renal involvement (64%) (Table 5) [22].

Agrawal et al, from CMC Vellore reported, fever (94.2%) as most common manifestation followed by renal manifestations (77.1%) [29]. In another study, done in 1994 with 201 children of SLE, (Table-6) LN was found in 84% of cases [30]. In another study renal disease was found to be the most common presenting feature of pediatric SLE [31].

Table 5: Clinical features of children with SLE in Asia [22]

Clinical features	Taiwan	Oman	China	Taiwan	Kuwait
Age at diagnosis (years)	13	8.6	-	13.5	10.7
Fever (%)	18.2	62	88.3	-	-
Weigh loss (%)	30	52	-	4.6	-
Alopecia (%)	20	36	-	13	-
Cutaneous rashes (%)	72	70	84.4	77	51
Mucosal (%)	40	10	-	26	29
Arthritis/arthralgia (%)	53	76	-	57	43
Hematological (%)	72	68	67.5	79.7	34
Leukopenia	38	14	-	34.6	-
Lymphopenia	32	16	-	58.8	-
Hemolytic anemia	56.2	60	-	44.4	20
Thrombocytopenia	19.7	20	-	19.6	23
Renal involvement (%)	81	64	76.6	58.8	29
Pulmonary (%)	9	26	-	-	9
Pleural effusion	9	14	-	15	-
Pneumonitis	-	16	-	-	-
Cardiac (%)	8	10	-	5.2	6
Neuropsychiatric (%)	34.5	18	37.3	34.6	14
Headache	-	-	31.8	-	-
Seizure	28	-	29.1	24.4	-
Psychosis	5	-	-	21.9	-
Stroke	-	-	-	-	-
Chorea	1.5	-	-	28.1	-

Table 6: Presenting symptoms of SLE in children [30]

Malaise, weight loss, growth retardation	96%
Cutaneous abnormalities	96%
Hematological abnormalities	91%
Fever	84%
Lupus nephritis	84%
Musculoskeletal complaints	82%
Pleural/pulmonary disease	67%
Hepatosplenomegaly and/or lymphadenopathy	58%
Neurological disease	49%
Other manifestations (cardiac, ocular, gastrointestinal, Raynaud's phenomenon)	13%-38%

Diagnosis

- Urine microscopy (hematuria, proteinuria, albuminuria)
- Leukopenia, anaemia, thrombocytopenia found during active disease should be monitored.
- Coagulation screen & DCT (to look for evidence of hemolysis)
- ANA is very sensitive for SLE (95-99%), but not very specific (~50%). ANA-negative lupus is extremely rare. Antibodies against ds-DNA and anti-Smith are specific for SLE (~98%) but not as sensitive (40-65%).
- Anti phospholipid antibody was found to be positive in 78% of cases in an observational study of Saudi Arabia, done between January 2002 and June 2014 [32].
- Anti-C1q antibody has high sensitivity (80%-100%) and specificity and both antibodies reflect the disease activity. The other antibodies (Anti-Sjögren's syndrome, Anti-Smith and anti-Sjögren's syndrome B) have variable sensitivity and specificity.
- Most LN children have antichromatin/ nucleosome antibodies (specificity - 98%; sensitivity 69%), and they may be positive when the anti-dsDNA antibodies are negative [33].
- Urinary biomarkers as fractional excretion of Endothelial-1 (ET-1), MCP-1, vascular cell adhesion molecule-1 (VCAM-1), may also be useful but require validations [34].
- Serum C3 and C4 levels are decreased.
- Percutaneous renal biopsy enables direct visualization, grading and classification which helps to guides selection of immunosuppressive therapies. It also provides disease activity index and chronicity index which further guides the need for increase in immunosuppressive therapy.

Indications of doing renal biopsy are renal involvement with reproducible proteinuria ≥ 0.5 g/ 24 h with haematuria, persisting isolated glomerular haematuria and/or cellular casts, persisting isolated glomerular haematuria, isolated leucocyturia (with exclusion of causes like infection or drugs) and unexplained renal insufficiency with normal urinary findings [35] . Different type of microscopy and their role are shown in Table 7.

Table 7: Microscopy with specific findings

Type of Microscopy	Function
Light microscopy	≥8 glomeruli should be examined with haematoxylin and eosin, periodic acid-Schiff, Masson's trichrome and silver stain [18]
Immunofluorescence or immunohistochemistry	Done for immunoglobulin and complement deposits (IgG, IgA, IgM, C3, C1q, κ and λ light chains) [36, 37]
Electron microscopy	Helps in recognition of proliferative and membranous lesions [38, 39, 40]

According to Consensus of the Brazilian Society of Rheumatology published in 2015, a renal biopsy should be done when serum creatinine is elevated with no apparent cause and associated with SLE, isolated proteinurea ≥ 1.0 g/24 h or proteinurea ≥ 0.5 g/24 h associated with glomerular dysmorphic hematuria and/or the presence of cellular casts [41].

Treatment [42]

There are six international guidelines along with KDIGO (Kidney Disease: Improving Global Outcomes) Glomerulonephritis Work Group from different geographical area (American, European, Spain, Netherland) published in 2012 with level of evidence for the management of LN in both adults and pediatric age group on the basis of trials conducted in the past 40 years [43]. Because of the lack of good prospective randomised control trials the treatment protocol used at various centres is same as that of adults [44]. Therefore, there is wide variation in treatment protocols at various centres. In 2008, first European League Against Rheumatism (EULAR) recommendations on the management of SLE were published [45]. In 2012, Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) gave recommendations for the management of adult and paediatric LN [44]. Treatment of LN is implemented in 2 stages, first is induction phase in which immunosuppressive therapy is given to produce clinical and serological remission (normalization of anti-DNA antibody and C3 C4 levels) and second is maintenance phase which is usually given after remission for 2-3 years.

Class I lesions - require no specific therapy.

Class II lesions – there is no specific therapy as there is very little evidence of the progression of the disease in further stages [46]. According to ACR

guidelines no immunosuppressive therapy is required. As per EULAR/ERA-EDTA oral glucocorticoids (0.25–0.5 mg/kg/day) can be given. Azathioprine (1–2 mg/kg/day), can be added with glucocorticoids as a steroid sparing agent, if proteinuria > 1 g/24 h with glomerular haematuria is present.

Class III, IV - KADIGO recommends initial therapy with corticosteroids, combined with either cyclophosphamide (CYC) or Mycophenolate mofetil (MMF). Addition of cyclophosphamide to corticosteroids for initial treatment decreases the frequency of kidney relapse, CKD and ESRD if compared to corticosteroids alone [47].

Oral prednisone with tapering according to clinical response over 6–12 months is the initial therapy. For severe cases, intravenous pulses of methylprednisolone should be given during 3 consecutive days @ 15–30 mg/kg/day or 600-1000 mg/m^2/day (maximum 1 g/day) and can be repeated depending on the severity of the disease. Methylprednisolone pulses should be followed by oral prednisolone (1–2 mg/ kg/day to a maximum dose of 60 mg /day) and tapered after 4-6 weeks on achieving remission to a dose of 0.5 mg/kg/day. Oral Cyclophosphamide (500-1000 mg/m^2 intravenous, monthly pulses for 6 months) should be added to this regimen to induce remission. Oral cyclophosphamide 1.0–1.5 mg/kg/d (maximum dose 150mg/d) for 2–4 months has been used as an alternative to i.v. cyclophosphamide with equivalent efficacy [48, 49]. After completion of induction phase, maintenance therapy with azathioprine or MMF, and low-dose oral corticosteroids should be given. KADIGO guidelines suggest continuation of maintenance theray for at least 1 year before consideration is given to taper the immunosuppressive therapy once the remission is achieved. If complete remission has not been achieved after 12 months of maintenance therapy, consider performing a repeat kidney biopsy before determining if a change in therapy is indicated. While maintenance therapy is being tapered, if kidney function deteriorates and/or proteinuria worsens, treatment should be increased to the previous level of immunosuppression that controlled the LN. The average duration of immunosuppression was 3.5 years in seven RCTs. [50,51, 52]. Therapy is monitored with serial measurements of proteinuria and SCr.

Class V lesions - Pure class V LN and persistent nephrotic proteinuria should be treated with corticosteroids plus an additional immunosuppressive agent like cyclophosphamide, calcineurin inhibitor, MMF or azathioprine. There have been no studies of the effect of treatment of class V LN on long-term kidney outcomes. Antiproteinuric and antihypertensive medications may reduce proteinuria by as much as 30–50% in class V LN [53, 54].

Class VI – Despite the absence of active LN, patients may still have extrarenal manifestations of systemic lupus requiring immunosuppression. Therefore child should be treated with corticosteroids and immunosuppressive therapy.

Members of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) after considering the existing medical evidence and current treatment approaches, formulated consensus treatment plans for induction therapy of newly-diagnosed proliferative LN. These guidelines were developed in three phases, first phase of the project consisted of an online Delphi survey that was sent to the 103 members of the CARRA SLE Disease Specific Committee and second phase consisted of a formal face-to-face consensus meeting with 32 elected by voting ,experienced pediatric rheumatologists, held over 2 days in April, 2010. Third phase done for finalization through the third Delphi survey with 216 (response rate 137/216=63%) members to achieve CARRA-wide consensus. Final consensus guidelines are shown in table no 8 [55].

Azathioprine is an immunosuppressive drug used in recurrent flare SLE patients when daily requirement of prednesolone is >15 mg [56]. Some international centres are using azathioprine as induction therapy, but outcomes are similar [57, 58]. Some meta-analyses showed superiority of MMF than to IV cyclophosphamide in term of response [59, 60]. But in a larger international randomized, controlled trial with 370 patients with classes III through V LN with both induction phase of 24 weeks and maintenance phase with tapering oral prednesolone

Table 8: CARRA consensus guidelines for treatment of LN [55]

Induction Phase	Immunosuppressive therapy	MMF 600 mg/m2/dose (max dose 1.5 gm, taken two times per day) **OR** i.v. Cyclophosphamide 500 mg/m2/month for 6 months (max dose 1.5 gm)
Maintenance Phase	Glucocorticoids	Oral Oral + i.v. i.v.

did not detect a significantly different response rate between the two groups: 56.2% patients responded to MMF compared with 53.0% in IV cyclophosphamide group [61].

Mycophenolate mofetil suppresses T and B cells which do not attack target organs but weakens the immunity. The ACR guidelines recommend MMF as the preferred agent for African Americans and Hispanics. In certain situations (black and Hispanic patients or to avoid premature ovarian failure), MMF is considered of first choice as induction therapy in LN [33, 34].

Rituximab (RTX) a chimeric monoclonal antibody specific for human CD20, may be effective in patients with WHO type IV LN resistant to conventional immunosuppressive therapies. ACR [62] as well as the EULAR guidelines [44] for the management of LN recommend the use of Rituximab as add on or as monotherapy with resistant disease. Few retrospective case series in children of Greece , Berlin , Germany too revealed the effective use of Rituximab in pediatric LN [63, 64].

Tacrolimus is a more effective Calcineurin inhibitor than cyclosporine and has a much better safety profile. Tacrolimus has been used in both induction as well as maintenance phase [65, 66]. Its role in pediatric lupus nephritis also been studied with good efficacy and safety profile [67].

As per all guidelines review use of hydroxychloroquine should be considered for all lupus patients. It is useful in children with marked skin disease, lethargy and arthritis. Annual eye screening, even in the absence of visual symptoms, is recommended as hydroxychloroquine causes macular toxicity and corneal changes [68]. Antimalarials, not only prevent lupus flares and increase long-term survival but also protect against irreversible organ damage [69, 70].

In very severe and refractory cases not responding to above medication, 5 -10 cycles of plasma exchanges can be considered with few positive outcome reports [71,72].

General Management

Dietary counselling should be done and supplementation with Vit D3, calcium rich diet should be given. Avoid nephrotoxic drugs and NSAIDS [73]. Monitoring of growth using growth charts and pubertal development assessment is important. ACE inhibitors and angiotensin II receptor blockers have been routinely used to treat proteinurea and associated hypertension in LN which helps in delay of kidney deterioration and cardiovascular disease [74,75]. Restrict fat intake or use lipid-lowering therapy such as statins for hyperlipidemia secondary to nephrotic syndrome. Restrict protein intake if renal function is significantly impaired.

Vaccination

Vaccination should be performed, before starting immunosuppressive therapy or if disease in inactive period. Vaccines that can be used are Pneumococcal (23-valent polysaccharide), Influenza, Diphtheria and tetanus (dT) and other inactive vaccines. Live virus vaccines like MMR and herpes zoster should be avoided. Immunisation should be done carefully as it may induce a disease flare [76,77,78,79,80].

Prognosis

With the evaluation of new therapies in the treatment of LN, survival and outcome has improved.

- Complete Response is demonstrated by an inactive urinary sediment, ≥ 50 % reduction in proteinuria to subnephrotic levels , decrease in proteinuria to ≤ 0.2 g/24 h and normal or near-normal GFR with stable renal function [74].
- Partial Response is a level of improvement, usually defined as an inactive sediment, proteinuria ≤ 0.5 g/24 h, with normal or near-normal GFR within 10% of normal GFR if previously abnormal (GFR > 90 mL/min/1.73m^2) or stable renal function with urine protein: creatinine ratio < 50 mg/mmol.
- Sustained Response of at least 3 to 6 months can be regarded as a remission but cannot be judged to be a complete remission in the absence of a biopsy [81].

Poor Prognostic Indicators

1. Delay in treatment of more than 5 months from onset of nephritis
2. Young age at onset of nephritis
3. Male gender
4. Black race
5. Hypertension
6. Nephrotic syndrome
7. Elevated creatinine level (> 3 mg/dL) at presentation
8. Persistently elevated anti-dsDNA and low C3 and C4 levels

9. Renal biopsy findings showing diffuse proliferative GN or high chronicity index.

Few disease activity indices have been developed to measure and validate reversible inflammation which include the British Isles Lupus Assessment Group (BILAG), European Consensus Lupus Activity Measurement (ECLAM), Systemic Lupus Activity Measure (SLAM), SLE Disease Activity Index (SLEDAI), revised versions as SLEDAI-2K and Safety of Estrogen in Lupus Erythematosus National Assessment (SELENA) SLEDAI. These indices are used for longitudinal observational studies as well as clinical trials [82].

At diagnosis and after one year patients with both renal and CNS disease had the highest SLE Disease Activity Index (SLEDAI) scores ($P < .0001$) [83].

Repeat renal biopsy at the end of induction is suggested in some studies for prognostic value [84, 85]. Complete remission rates at 6–12 months in various western studies with mixed races were between 8% and 30% [48, 61, 85]. But in Chinese clinical trials complete remission rate was between 60–80% [87, 88]. In a retrospective study of north India, over 20 years renal survival rate was 91%, 81% and 76% at 5, 10, and 15 years, respectively . And in the worst-case scenario, survival was 79%, 70%, and 66%, respectively at 5, 10, 15 years [89].

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Review Article

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Consent in Paediatrics

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Abstract

Consent means voluntary agreement, compliance or permission. Consent signifies acceptance by a person of the consequences of an act that is being carried out. Informed consent is a communication process of providing the patient/parents/guardians with relevant information regarding the treatment and the diagnosis, so that they can make informed decisions. The process of informed consent in pediatric patients is not well understood. The amount of information to be disclosed in an informed consent is a matter of debate.

Keywords: Consent; Assent; Child; India; Informed Consent; Parents.

Introduction

Informed consent is a communication process that is ethically required before initiation of any treatment or procedure. It provides relevant information regarding the diagnosis and treatment needs so that an educated decision can be made. This is required for all aspects of medical care including preventive, diagnostic and therapeutic measures, and research. Consent is considered valid or real when it is given voluntary without coercion, given by person with capacity and competence to give consent and has minimum level of adequate information about the nature of procedure to which he/she is consenting [1].

Reasons for Obtaining Consent

It respects the autonomy of the individual and protects the patient from any form of physical or psychological harm. It is also considered a legal document to protect the practitioner from claims associated with miscommunication [2].

Types of Consent

Expressed (specifically stated by the patient) Oral: Oral consent should be taken in the presence of uninterested third party. Mainly in cases where intimate examination of female is required. Tests necessitating removal of body fluids, radiological examination can be done after securing oral consent. Written: It is advisable to take written consent in the presence of disinterested third party (this third party is only to attest the signature of the patient). Written consent is mandatory in every invasive diagnostic/therapeutic procedures or any medico legal examination [3].

Components of Consent

An informed consent can be either general or specific. A general consent for treatment is obtained for physical examination, basic investigations and prescription of standard medications. Procedures and treatment considered a part of routine medical work up like administration of drugs or routine X- ray or blood investigations and intravenous cannulation do not require written consent [4].

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Informed Consent Guidelines for Immunization

Purpose: To guide immunization providers in developing their own policies and procedures regarding informed consent for immunizations, To ensure all are informed before receiving immunization. This information should include that all immunizations are voluntary. It is the ethical and legal responsibility of the immunization provider to obtain the informed consent. The need to obtain informed consent prior to an immunization is based on the principle that a client is autonomous and has the right to determine what happens or does not happen to them. Information, comprehension and willingness to participate (voluntariness) are fundamental elements of the informed consent document. The consent should adequately convey all the information needed for the subject to understand the immunization event, in addition to being in a language understandable to the client. A client's consent to participate must be free from coercion. Above all, the client should be able to understand the information presented in order to make an informed decision [5].

Who can Give Consent

As per Indian Majority Act, Guardian and Wards Act, and Indian Contract Act majority is achieved at an age of 18 years and considered a legal age for giving a valid consent for treatment. A child below 12 years (minor) cannot give consent, and parents/ guardian can consent for their medical/surgical procedure. A child between 12-18 years can give consent only for medical examination but not for any procedure. Orphans or unknown or street children, the court is appointed as a guardian and any procedures/treatment requires court permission. In case of emergency, when parents/guardians are not available to consent, a person in charge of the child like principal or school teacher can consent for medical treatment (Loco parentis). A legal age of 18 years has been set to consent for termination of pregnancy (MTP Act1971) and for Donation of blood and donation of organs (Transplantation of Human Organ Act 1994) [5].

Who should Obtain the Consent

The physician rendering the care may obtain the consent himself. Staff nurses or other health care providers are not entitled to obtain the consent although they can bridge the communication gap between the physician and the patient [6].

Elements of Informed Consent

It must be written in patient's understandable language & must not include too many medical terminologies. It should explain the nature of the ailment/ disease & its available treatment modalities including alternative treatment options. It should explain nature of the proposed procedure, its inherent risk, sequelae and potential benefits and prognosis of the patient with and without the proposed treatment. It must identify the attending physicians/ unit in-charge/ hospital name & address. It must mention the date/time/place and number of witnesses. An acknowledgment that no guarantee and promises has been made to the parents concerning the result of any procedure. Assessment of parental understanding of the information that has been provided and that their queries have been answered to their satisfaction. Assurance that parents have the freedom to choose among the medical alternatives without manipulation. It must be comprehensive and readable with short and simple sentences [7].

Legal Implications of Informed Consent

Treating a patient without consent constitutes a battery, and failure of adequate disclosure amounts to negligence. Framework under which patient can obtain redressal for their injuries resulting from consent include criminal penal code (IPC-Indian Penal Code), Medical Council Act, and Consumer Protection Act (COPRA) [8].

As per the Indian Contract Act, if one party to the contract is misled or has entered into it in a different sense to that in which it ought to have been understood, then it would not be construed as a valid contract. Under the Indian Penal Code (IPC) 1860, Section 89 stipulates that an act done in good faith for benefit of a person under 12 years of age by consent, either express or implied, by the guardian or other person having lawful charge is not an offence by reason of any harm. This exception is not available if there is an intention to cause death or grievous hurt. In emergency situations, where there are no guardians/parents from whom it is possible to obtain consent, one can proceed to save the life of the child (Section 92 IPC) [8].

Medical Council of India (MCI) considers failure to obtain consent (from the parents/guardian in case of minors) prior to surgical treatment as misconduct. If the practitioner is found guilty, the Council may award the punishment as necessary and may direct the removal of their name altogether/temporarily from the register [8].

COPRA has emerged as weapon against unlawful medical practices in India and happens to be only social forum for the patients who are subjected to unethical medical practices. A main drawback with COPRA is that it has no provision to punish people who file unnecessary and false cases against the doctors [8].

Definition of Terms Related to Informed Consent

Consent By Proxy: Informed permission given by the parents or legal guardian as an authority and a responsibility to safeguard the welfare and best interest of their issue [4,5].

Informed Assent: Child's agreement to medical procedures in circumstances where he or she is not legally authorized or lacks sufficient understanding for giving consent competently [5].

Implied Consent: When the parents bring their child to a physician for treatment of any ailment it implies that they are agreeing for their child to go through the medical examination in the general sense [5].

Expressed Consent: When a patient specifically grants the physician permission to undertake the diagnosis and treatment of a specific problem. It may be an oral or a signature/written consent [6].

Valid Informed Consent: Consent with emphasis on patient's understanding of the reasonanble and irrational elements of his/her decision [6].

Rules of Consent: Oral consent should be obtained in the presence of a disinterested third party (nurse). In criminal cases, the victim cannot be examined without his/her consent. The child under 12 years of age and an insane person cannot give valid consent to suffer any harm (Section 89. IPC). Consent is not a defense in cases of professional negligence. A person above 18 yrs of age can give consent to suffer any harm if the act is not intended and not known to cause death or grievous hurt.(section 87 IPC) [9].

Dealing with Refusal to Consent: When the parents/guardian refuse to undergo the desired diagnostic procedure/treatment after a complete and comprehensive information has been provided, they should be informed in a discreet professional manner of consequences of refusal, failing which the physician can be held liable in the court of law. The conflict of 'best interest standards' for treatment of the child versus 'rational parent standard' for the attitude of parents is matter of never ending debate [10].

In the absence of an emergency, it is generally agreed that parents have a right to refuse treatment. However, it remains unsettled as to what should a physician do when a part of medical treatment is refused. For example, if the parents refuse for a lumbar puncture in a child with suspected meningitis, but consent to all other blood investigations and treatment. No court of law can protect the physician from litigations if he denies treatment on such grounds [10].

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Article in supplement or special issue

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