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The **second page** should contain the full title (without the name of the authors), abstract not exceeding 200 words, and three to ten key words. The abstract should clearly describe the aim of the study, important findings and implications.

The **text should begin from page 3** under the headings: Introduction, Material and Method, Results and Discussion.

References and Appendix should follow on separate pages. Each table should be on separate page, numbered with Arabic numerals and provided with a short descriptive title. The findings of the tables should not be repeated in the text.

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These should be brief not more than **1000 words in length with a maximum of 10 references.** First page and second page (with abstract) should be same as for full-length articles.

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The maximum permissible length for letters **is 500 words with a maximum of 5 references**; tables and figures cannot be used. Letters can be in reference to articles published in this journal, or any other significant matter.

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[1] J. van der Geer, J.A.J. Hanraads, R.A. Lupton, The art of writing a scientific article, J. Sci. Commun. 163 (2010) 51–59.

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Editorial

Free Radicals are dutiful soldiers, no more to be spared as bio-terrorists

Arambam Giridhari Singh
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DOI: http://dx.doi.org/10.3126/jonmc.v6i2.19561

If we analyse the increasing beneficial roles so far explored as being played by free radicals and their deliberate enzymatic generation when requied, one can very well presume their generating pathways as inteligently designed systems already existing for maintaining normal health. On the other hand, free radicals, if produced in excess because of various unwanted exogenous factors,they begin to covet their neighbouring molecules' electrons and by stealing electrons, they operate as terrorists by producing diseases in the body. The idea of constructing this title of the editorial came suddenly to the mind of the author after having a glimpse of a very recent article (Dec 2016), the main cotent being the emergence of molecular hydrogen as top ranking antioxidant.possesing the full potentiality of minimizing excssively generated free radicals upto its physiological level.

Before jumping directly on to those documented facts and other reports for support of the title of the editorial, let us have a briefing on free radicals to refresh the knowledge we conceived earlier. Free radicals are those molecular species capable of independent existance, each containing an unpaired electron in one of their atomic orbitals, hence very reactive and short-lived. Some species without unpaired electrons like, singlet oxygen, hydrogen peroxide etc. which can easily be transformed to the most reactive species have also been taken in as their members under a class known as reactive oxygen species (ROS). Thus, we have two groups of free radicals namely, (1) reactive oxygen species (ROS) and (2) reactive nitrorgen species (RNS). Reactive oxygen species are partially reduced derivatives of molecular oxygen and in this group, we have Singlet **oxygen ($^1O_2$), Superoxide anion radical ($\cdot O_2^-$), hydroxyl radical ($^{\cdot}OH$), hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl**) etc as its important members. **Hydroxyl radical (OH$\cdot$)** and **hypochlorous acid (HOCl**) are the most reactive members directly involved in damaging tissues or molecules. **Nitric oxide ($\cdot NO$**) is the mother molecule of RNS, the other members of this group namely, **nitrous oxide (N_2O), Peroxy nitrite ($^{\cdot}OONO$), nitrogen dioxide ($\cdot NO_2$), nitroxyl anion (HNO), peroxy nitrous acid (HNO_2**) etc are all derivatives of **$\cdot NO$. Peroxynitrite (OONO**) is the most reactive nitrogen species which can direcly react with various biological target molecules.

Endogenous sources of free radicals are **(a)NADPH oxydase, being an enzyme dedicated for generation of ROS** in mammalian cells from NADPH as its substrate **(b) Nitric oxide synthase** (NOS), also being an enzyme dedicated for synthesis of nitric oxide ($\cdot NO$), the mother molecule of RNS, the substrates being Arginine and molecular oxygen, **(c)Energy pathways**, mitochondrial electron transport chain being the most delicate site of energy pathway where highest quantity of superoxide anion radical can be generated, **(d) Oxidases**, utilising molecular oxygen as co-factor, most of the time being associated with the production of H_2O_2,**(e)Exercise,** because of increased flow of oxygen,in the skeletal muscle, folowed by increased ETC and xanthine oxidase activity.**(f)**.**Peroxysomes** being organelles producing

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H_2O_2 as byproducts of degaradation of fatty acids and other molecules in it..Free radicals generated by the endogenous pathways, if maintained at its physiological levels, are always found to be engaged in beneficial pathways.

Free radicals: To be treated as dutiful soldiers This first part of the title of the editorial can now be supported by the following few crucial roles, documented as being played by endogenously generated free radicals. **(1) Defence against foreign invaders:** Our body harnesses the most dangerous free radicals for use in the immune system for defence against pathogens. Certain cells like neutrophills, macrophages etc, engulf bacteria or viruses and creats the most powerful free radicals like hypochlorous acid (HOCl) or hydroxyl radical (OH) by taking up molecular oxygen (O2) rapidly from the blood for bombarding the pathogens. NADPH oxidase play the dmnant role in producing the initial ROS

$$2O_2 + 2\ NADPH \xrightarrow{NADPH\ \ Oxidase} 2 \cdot O_2^- + NADP + H+$$

$$2 \cdot O_2^- + 2H^+ \xrightarrow{Superoxide\ -dismutase} H_2O_2 + O_2$$

$$H_2O_2 + Cl- + H^+ \xrightarrow{Myloperoxidase} HOCl + H_2O$$

$$H_2O_2 + Fe++ \xrightarrow{Fanton\ reaction} \cdot OH + OH^- + Fe+++$$

(2) NO as signalling agents: The most well-known free radical acting as signalling molecule is ▪ NO. Three isoforms of NOS are available for synthesis of three ▪ NO radicals having different signalling characters. The gene for NOS-1 or nNOS(neuronal NOS) is located in chromosome no. 12. The role of NO synthesised by NOS-1 works for cell to cell communication. The gene for NOS-2 or iNOS(inducible NOS) is located in chrosome no.17 and ▪ NO synthesised by it is involved in defense against pathogens after conversion to highly reactive free radical namely peroxy nitrite(OONO). The gene for NOS-3 or eNOS (endothelial NOS) is located in chromosome No. 7 in endothelial cells, endocardium and myocardium, in plasma membrane and it is activated by calcium. ▪ NO synthesiized by it is involved in muscle relaxation by using cGMP as its 2nd messanger [1]. **(3) Regulation of sperm function:** Free radicals, at its physiological level, control the maturation, capacitation, hyperactivation, the acrosome reaction (AR) and oocyte fussion of sperms. Lipid peroxidation caused by low level of reactive oxygen species leads to modification of plasma membrane facilitating sperm oocyte adhesion [3]. **(4) Acting as signal substance for regulating heart beat:** When our body is subjected to different types of stress, symphatatic nervous system starts stimulating β adrenergic receptors on the surface of the heart muscle cells leading to contraction of the heart with greater force via activation of certain proteins inside the cells by phosphorylation.It was also found that these β adrenergic receptors, ,when stimulated, caused increased production of free radicals in the mitochondria of the cell and these then contribute to stronger contraction of the cells. This β adrenergic stimulation of heart muscle cell disappeared when exposed to antioxidants showing the real role of free radicals for pumping more blood by the heart in stress filled situations and negative effect of antioxidants [4]. **(5) Regulation of Erythropoietin production**: Production of erythropoietin (EPO), the glycoprotein hormone which control red blood cell formation has already been reported as being regulated by ROS by feedback mechanism. H_2O_2, via production of OH by Fenton reaction, could act as intracellular signalling molecule. High cellular level of H_2O_2 inhibit EPO production while low levels, as under hypoxia, allow full expression [2]. **(6) Enhancement of insulin sensitivity:.**Free radicals induced by exercise enhances insulin sensitivity via activation of free radical dependent trancriptional co-factors and transcription factors. This free radical related induction of transcription factors and transcriptional co-factors, also lead to increased expression of enzyme antioxidants including **superoxide** dismutase-1(SOD 1), superoxide dismutase-2(SOD 2) and glutathion peroxidase, thus, offering an increased protection from

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oxidative stress [6]. **Exogenous** sources of free radicals are (a) Alcohol **consumption**, (b) **Tobacco smoking**, (c) **Ingestion of heavy and transition metal ions, industrial solvants, pesticides** etc (d) **Toxic drugs** while detoxifying by **cytochrome 450** (e**) Exposure to ionizing radiation, ozone, poluted environment hyperoxia** etc. Free radicals produced under exogenous conditions, always intends to overwhelmed body's ability to regulate them ultimately leading to a condition known as oxidative stress. All aerobic forms of life, as such, maintained an elaborate antioxidant system as its own defense squad; enzymes like superoxide dismutase (SOD), catalase and glutathione peroxidase and non-enzymic molecules like glutathione ,uric acid, allopurinol etc, being its membersnt squad fails to counteract the increasing load of free radicals, because of their attack on DNA, protein, and lipids in the body,the consequeces will be the appearance of diseases like,cancer, atheroschlerosis, heart disease, cardiovascular disease, stroke, emphysema, diabetes mellitus, rhumatoid athritis , osteoporosis, ulcers, sun burn, cataract, Crohn's disease, aging etc. Under such conditions, antioxidant therapy will be the only option but, despite the current wealth of knowldge on exogenous antioxidants, there was much skepticism regarding the likelihood of a complete success with the so far existing standards of antioxidant therapy.

Free radicals: no more to be spared as biological terrorists As cited above, this last part of the title of the editorial was inserted after getting sufficient supportive information from Lei Huang's recent article, appeared in Medical Gas Research 2016 [7], the impotant information being about **molecular hydrogen appearing** as the most promising antioxidant which could be used both for preventive and therapeutic treatment of almost all types of free radical linked diseases. The underlying comprehensive mechanism of this gas is beyond hydrxyl radical scavenging. Uptodate clinical application of this gas to human patient conducted so far, also revealed the safety and promising benefits in varieties of diseases. The commendable characteristics of **molecular hydrogen** they have discovered,ensuring the feasibility and readiness of its clinical translation to human patients are (a) nontoxicity even at very high concentrtion, (b) diffusibility into the subcellular compartments to reduce the cytotoxic oxy- radicals, (c) mild nature, neither disturbing metabolic redox reactions nor affectng signalling ROS , (d) ability to act selectively on the most reactive hydroxyl radical, (e) regulating gene expression, (f) acting as noble signalling molecule , (g) triggering the activation or upgradation of the endogenous antioxidant enzymes, (h) ability to cross blood brain barrier (i) and its capability of imparting the highest antioxidant dose.

Conclusion: So long the concentration of the free radicals generated endogenously remain maintained at its physiological level, almost all of them will remain engaged in body's beneficial activities. Slight excess if any, will also be taken care of by the antioxdant squad created endogenously. But, because of our own ignorance or negligence, if we keep on indulging or exposing ourselves to those unwanted exogenous conditions mention above, oxidative stress will automatically be developed due to the extra load of free radicals, the concequence of which being, the appearance of different diseases. Under such condition, interuption by antioxidant therapy may be the only option. Till now, this effort of trial with antioxidant therapy is going on without much significant response except for a very few cases. However, after this recent discovery of molecular hydrogen as the best antioxidnt tested so far, a new hope suddenly emerges, with full confidence of overcoming all the obstacles being faced while conducting clinical trials of different antioxidants. I wish all the researchers working under this project a great success for the sake of those patients still waiting for recovery. As such, as per the message from Molecular Hydrogen Foundation

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(MHF), we can safely start consuming molecular hydrogen (H2) in place other antioxidants, as H2 only reduces excessive oxidative stress and does not interfere with beneficial ROS.

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Original Article

Study of housing conditions among people of a rural community in Morang, Eastern Nepal.

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Abstract

Background

Poor Housing condition, sanitation and hygiene is associated with adverse health conditions. This study is done to assess the housing conditions, sanitation coverage and hygiene practices among rural community in Bhaudaha VDC, eastern Nepal.

Material &Methods

A cross sectional study was conducted from 22nd May 2016 to 22nd November 2016 in Bhaudaha VDC of eastern Nepal with appropriated sample size of 525 participants. A direct interview was taken with structured questionnaire. Chi square test was used to find out association of the variables.

Results

Out of 525 respondents, adequate ventilation was present among 54.9% literates followed by 44.2% illiterates (p=0.01) and separate kitchen was also found among 77.2% of literates and 64.6% of illiterates (p=0.002). Among Dalit castes 74.4% had separate kitchen in their house followed by 50.7% janajatis (p<0.001). Covering of stored water was found in 75.8% Dalit and 61.2% Janajati (P=0.003). Improved sanitation was highest among other terai casts (78.1%) followed by Dalits (59.9%) and 58.2% Janajati (p=0.132).

Conclusion

There is need of appropriate methods of health education to be focused on all the groups in the community for improvement in sanitation and healthy housing conditions and targeted more towards Janajati and illiterate group and further studies need to be done in different region of Nepal to understand the cause of disparities in housing and sanitation conditions among different groups.

Keyword:
Community, Health, Housing, Sanitation

Introduction

Providing a safe and healthy environment for the inhabitants is an interpretation of healthy housing. Technical, social, planning and policy factors are related to housing which affects physical, mental health and social wellbeing. In terms of basic human requirements that form housing standards, policies and goals of attainment relevant to an individual country's needs, these factors are expressed. Around two third of our life is spent in home and its immediate surroundings. Each of us is potentially at risk from an insanitary or unhealthy housing environment. Moreover, vulnerable groups like children, mothers with young children, the elderly, disabled persons, the chronically sick and the unemployed can be

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disproportionately affected by poor housing conditions and usually have special health and housing needs. [1].

On the basis of materials used in the construction of building, characteristics of housing has changed over the past 15 years in Nepal. However, the Population using latrine has more than doubled during this period [2]. Reports of WHO and UNICEF (2004) showed that South Asia is not on track to meet the Millennium Development Goal (MDG) for sanitation [3]. Joint Monitoring Program (JMP) of UNICEF and WHO has defined improved sanitation facility as one that hygienically separates human excreta from human contact. The coverage of sanitation in rural area is only 37% and an urban area is 78%. This shows that there is big disparity between urban and rural sanitation. Nepal has target of universal coverage by 2017 [4]. According to estimation of government, 62% has access to basic sanitation facilities. Although Nepal is in progress to the MDG target for sanitation, there are challenges in making sanitation facilities available for unreached people. Major challenges are the lack of adequate financial resource and skilled person willing to work in rural areas, lack of appropriate and affordable technologies, and lack of energy despite of huge potential for hydropower [5].

Objective

The objective of this study is to assess the housing conditions, sanitation and hygienic practices among rural community in Bhaudaha VDC of Morang district, Eastern Nepal.

Materials and Methods

A cross-sectional study was carried out in Bhaudaha VDC of Morang District. The study was conducted in the VDC of study population 1,605 from 9 wards. The study period was from 22nd May 2016 to 22nd November 2016 and conducted after the approval of Institutional review committee (IRC).

Sample Size

The sample size was calculated on the basis of 76.1% of kachha and semi pucca houses (including 51.6% mud bonded and 24.5% wooden pillar foundation) in rural Nepal (Annual Household Survey 2014/15) [6]. Considering permissible error of 5% of the proportion, 5% level of significance and using the formula $n = Z^2PQ/L^2$ = 1.96X1.96X76.1X23.9/3.81X3.81 = 481.33, the final sample size was determined as 529 after adding 10% for non response error. The samples were chosen randomly from 9 different wards but 4 respondents denied to take part in the study. Thus only 525 participants were included in study.

Data collection

For data collection, pretested structured questionnaire was used and face to face interview was conducted with one member of each household who were atleast18 years or elder and either owner of the house or family of the owner. Interview was conducted only after taking verbal consent from the respondents and each respondent was explained the purpose of the study before interview. Written permission was also taken from the VDC. For grouping communities into caste groups like dalit caste, Janajati or other terai castes, Population Monograph of Nepal was used [7]. Houses were classified according to materials used for construction as Kachha, Semi-pucca and Pucca [8].

Data entry and analysis

Data entry was done using Microsoft excel. Data were analyzed using SPSS version 16. Chi-square test was used to find associations among different variables. A p-value less than 0.05 were considered as statistical significance.

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Result

In this study, out of 525 household respondents that were interviewed, 37.1% were below 30 years of age and remaining were 31-90 years of age. Among the participants in the study group 63.8% were female and 60.8% could not read or write and 38.3% were employed. Type of family was mostly nuclear 62.7% and land holding of more than 1 kattha was 67.2% among the participants. Dalit castes were 68.4% among the participants followed by 25.5% janajatis and 6.1% other terai castes.

Table.1. Demographic Characteristics of respondent of household (N= 525)

Characteristics	N	%
Age Group		
18-30 yrs	195	37.1
>30 yrs	330	62.9
Sex		
Male	190	36.2
Female	335	63.8
Literacy Status		
Literate	206	39.2
Unable to read and write	319	60.8
Employment Status		
Employed	201	38.3
Unemployed	324	61.7
Type of Family		
Nuclear	329	62.7
Joint	196	37.3
Land Holding		
<1 Kattha	172	32.8
>1 Kattha	353	67.2
Caste/Ethnicity		
JanaJati cast	134	25.5
Dalit cast	359	68.4
Other casts	32	6.1
House type		
Kachha	347	66.1
Semi-pucca	127	24.2
Pucca	51	9.7
Sanitation		
Improved sanitation	318	60.57
Unimproved sanitation	165	31.43
No toilet facility	42	8.0

Housing characteristics observed regarding construction were 66.10% Kachha house, 24.2% semi pucca house and 9.7% pucca house. Pucca house was observed in 16.0% literates followed by 5.6% illiterates while 71.2% of those who did not know to read or write had kachha house ($p<0.01$). The study showed 13.0% who had land holding more than 1 kattha had pucca house and semi pucca house was observed in 26.9% followed by only 2.9% pucca house among land holding less than 1 kattha while 78.5% of <1 kattha group and 60.1% >1 kattha group had kachha house ($p<0.01$). Among the participants who were not able to read and write, 55.8% did not have ventilation in their house followed by literates (45.1). Similarly, 52% among nuclear family did not have ventilation followed by 51% among joint family. Similarly, 59.3% among those who had land holding less than 1 kattha did not have ventilation followed by 47.9% among more than 1 kattha ($p=0.01$). Similarly, separate kitchen and bathroom was not found among 35.4% Illiterates followed by 22.8% literates ($P=0.002$). In the study people dwelling in up to 2 rooms were observed in 27.7% kachha house in the community while 3-4 rooms were observed in 66.7% pucca house followed by 64.6% kachha house and 61.6% semi pucca house ($p<0.001$). However, 27.0% Dalit castes live in up to 2 rooms in the community followed by 18.8% other terai cast and by 16.4% Janajati ($p=0.11$).

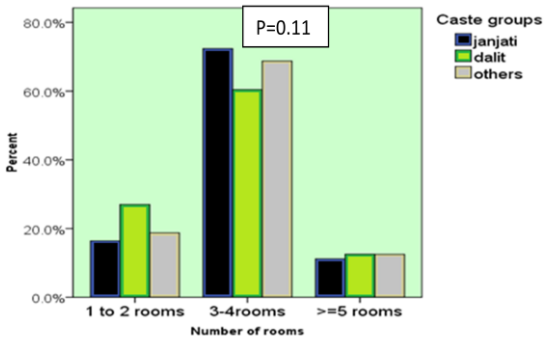

Fig.2.Distribution of rooms among different caste group.

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In the community only 8.00% of the study group did not have latrine facility at their home However, Improved sanitation was highest among other terai casts (78.1%) followed by Dalits (59.9%) and 58.2% (p=0.132). Water supply in the latrine was found in 44.3% of dalit caste followed by 36.6% janajatis and only 25.0% other terai castes (p=0.082). Among the caste groups, hand washing before meal was seen more among other terai castes 100% followed by 98.6 % dalit and 83.6% Janajati; while soap and water for hand washing was seen more among 81.1% dalit followed by 76.1% Janajati and 71.9 % other terai castes.Also 29.8% of illiterates did not cover the water while storing it followed by 24.3% literates.

Among Dalit castes 74.4% had separate kitchen in their house followed by 50.7% janajatis; however, 93.8% of other castes had separate kitchen in their house (p<0.001. Storage of water in plastic bucket was seen more among dalit castes (84.7%) followed by other terai castes (81.2%) and 70.1% of janajatis (P=0.01). However, covering of stored water was seen more among other terai castes (81.2%) followed by 75.8% dalit and only 61.2% Janajati (P=0.003).

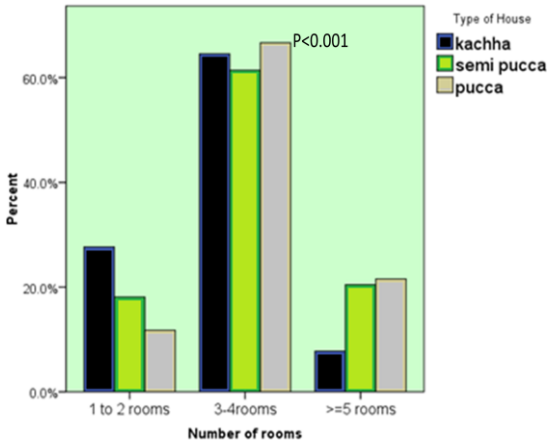

Fig.3. Number of rooms according to type of house.

Table.2. Relation of Hand washing and sanitation practices according to Literacy status (N=525)

Characteristics	Hand washing After meal			p value	Sanitation			p value
Literacy Status	**No washing**	**Wash with water only**	**Wash with Soap and water**		**No Latrine**	**Improved**	**Unimproved**	
Literate	9 (4.4)	23 (11.2%)	174 (85.5%)	0.053	8 (3.9)	149 (72.3)	49 (23.8)	
Unable to read and write	18 (5.6)	59 (8.9%)	242 (75.9%)		34 (10.7)	169 (53.0)	116 (36.4)	<0.001

Table.3. Housing condition as observed in the community (N= 525).

Variables	Ventilation		P value	Separate kitchen/Bathroom		P value	Type of House			P Value
	Yes	**No**		**Yes**	**No**		**Kachha**	**Semi Pucca**	**Pucca**	
Literacy status										
Unable to Read and write	141 (44.2)	178 (55.8)	0.01	206 (64.6)	113 (35.4)	0.002	227 (71.2)	74 (23.2)	18 (5.6)	<0.001

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Literate	113 (54.9)	93 (45.1)		159 (77.2)	47 (22.8)		120 (58.3)	53 (25.7)	33 (16.0)	
Type of family										
Nuclear	158 (48.0)	171 (52)	0.8 5	227 (69.0)	102 (31.0)	0.7 3	226 (68.7)	75 (22.8)	28 (8.5)	0.23
Joint	96 (49.0)	100 (51)		138 (70.4)	58 (29.6)		121 (61.7)	52 (26.5)	23 (11.7)	
Land holding										
>1 kattha	184 (52.1)	169 (47.9)	0.0 1	249 (70.5)	104 (29.5)	0.4 6	212 (60.1)	95 (26.9)	46 (13.0)	<0. 001
<1 Kattha	70 (40.7)	102 (59.3)		116 (67.4)	56 (32.6)		135 (78.5)	32 (18.6)	5 (2.9)	

Table.4. Housing condition, Sanitation practices and hygiene among caste groups in the community (N=525)

Variables	**Caste groups**			**P value**
	Janajati	**Dalit**	**Other terai caste**	
Sanitation				
No Latrine	15 (11.2)	25 (7.0)	2 (6.2)	0.132
Improved Sanitation	78 (58.2)	215 (59.9)	25 (78.1)	
Unimproved Sanitation	41 (30.6)	119 (33.1)	5 (15.6)	
Water supply in Toilet				
No Latrine	15 (11.2)	25 (7.0)	2 (6.2)	
Water supply Present	49 (36.6)	159 (44.3)	8 (25.0)	0.082
Water supply Absent	70 (52.2)	175 (48.7)	22 (68.8)	
Distance of water source				
Far >500 m	1 (0.7)	34 (9.5)	2 (6.2)	
Near <500m	133 (99.3)	325 (90.5)	30 (93.8)	0.001
Hand washing Before food				
Yes	112 (83.6)	354 (98.6)	32 (100)	
No	22 (16.4)	5 (1.4)	0	
What do you use to wash hands normally?				
Don't wash after meal	22 (16.4)	5 (1.4)	0	
Water only	10 (7.5)	63 (17.5)	9 (28.1)	
Soap and water	102(76.1)	291(81.1)	23 (71.9)	
Storage of water				
Muddy pot	5 (3.7)	17 (4.7)	2 (6.2)	0.001
Plastic bucket	94 (70.1)	304 (84.7)	26 (81.2)	
Other	35 (26.1)	38 (10.6)	4 (12.5)	

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Cover stored water				
Yes	82 (61.2)	272 (75.8)	26 (81.2)	
No	52 (38.8)	87 (24.2)	6 (18.8)	0.003
House type				
Kachha	84 (62.7)	245 (68.2)	18 (56.2)	
Semi pucca	40 (29.9)	78 (21.7)	9 (28.1)	0.19
Pucca	10 (7.5)	36 (10.0)	5 (15.6)	
Separate Kitchen/Bathroom				<0.001
Yes	68 (50.7)	267 (74.4)	30 (93.8)	
No	66 (49.3)	92 (25.6)	2 (6.2)	
Ventilation				
Yes	57 (42.5)	178 (49.6)	19 (59.4)	0.169
No	77 (57.5)	181 (50.4)	13 (40.6)	

Discussion

More than half of the households in our neighbouring country India live in kachha/semipucca (14% kachha, 40% semipucca) houses while most of the illness in India is due to poor environmental sanitation conditions [9].

In this study 66.10% of the study group in rural setting dwell in Kachha house followed by 24.2% semi pucca house and 9.7% pucca house. The result was similar to 56.95% kachha roofing and 91.22% kachha wall house as revealed in National Population and Housing Census 2011 of Morang [10].

In this study, among those living in Kachha house, maximum was Dalit caste (68.2%), followed by 62.7% janajati and 56.2% other terai castes. In a similar study of Housing Condition in Kerala with special focus on rural areas and Socially Disadvantaged Sections showed different results as 29.36% scheduled caste had kachha materials used to build walls while materials used to build roof were 48.77% tiles and 6.33% used kachha materials in roof. In same study only 3% scheduled tribes had kachha roof and 34.63% had roofs of tiles while 26.73% scheduled tribes used kachha walls; concrete was used for building only by 24.92% of Scheduled tribes and 24.30% of scheduled caste groups in Kerela [11]. However, in a different study of caste-based discrimination in Bangladesh, 76 per cent for Hindu Dalits and 91 per cent for the Muslim Dalits live in Kachha houses and about 14 per cent of Hindu Dalits and 8 percent of Muslim Dalits live in semi-pucca houses and 99 per cent live in 1-2 room houses [12]. In this study however 27.0% Dalit castes live in up to 2 rooms in the community followed by 18.8% other terai cast and by 16.4% Janajati , though not statistically significant ($p=0.110$) .

According to research done by WaterAid (2011), water, sanitation and hygiene (WASH) related mortality observed in Nepal were 14% child deaths due to diarrhoea. Study shows that Sanitation access lowered children suffering from diarrhoea by 7-17%, and reduced mortality for children under five by 5-20%. This shows the impact of WASH on public health [13].

In this study, 92% household had latrine facility at their home where Improved sanitation was highest among other terai casts (78.1%) followed by Dalits (59.9%) and 58.2% Janajati ($p=0.132$) and Improved sanitation coverage within whole

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community was 60.57%. Water supply in the latrine was found in 44.3% of dalit caste followed by 36.6% janajatis and only 25.0% other terai castes (p=0.082). In a different study done by Acharya P. et.al. in slums of Pokhara, 96.3% had toilet facility in home with 77% improved latrine. [14]. However, demographic survey of government (2016) has revealed that 62.9% of Nepalese rural households have improved sanitation facilities which is the marked improvement made in 5 years time [15]. This shows there have been focused programs among marginalised community for improvement of basic housing requirement like sanitation by the government.

In this study, hand washing with soap and water was observed more among literates (85.5%) however 75.9% of people who were not able to read and write also washed hands with soap and water (p=0.053). In a different study done in Odisha, India, among urban slum children and their care takers, 72% women washed hands with soap after toilet [16].

In this study, 74.4% Dalit castes had separate kitchen in their house followed by 50.7% janajatis, although maximum of otherterai castes (93.8%) had separate kitchen in their house (p<0.001), this shows that all the caste group have better housing practices with regards to separate kitchen. In Kerela, study of Disadvantaged people 93.19% Scheduled caste and 88.43% of scheduled tribe had separate kitchen in their dwelling [11].

In this study, covering of stored water vessels was seen 81.2% among other terai castes followed by 75.8% dalit and only 61.2% Janajati (P=0.003). In a report of 2000, 53.0% rural household and 48.5% Eastern terai household covered the vessels of stored water in Nepal [17].

Conclusion

Study shows that there is need of awareness programs to be focused on improvement in housing and sanitation conditions among all the groups in the community, which has to be targeted more towards Janajati and illiterate group. The rural regions of Nepal still have poor housing conditions in terms of materials used for construction of houses and use of improved sanitation; hence there is need of more such studies to find out the cause of disparities in housing and sanitation conditions among different groups in rural communities in Eastern Nepal for implementation of proper public health programs.

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Original Article

Utility of Epworth Sleepiness Scale (ESS) in predicting the presence of Sleep Related Breathing Disorders (SRBD) in patients in Routine Respiratory Clinical Service

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Abstract

Background

Many patients attending routine respiratory clinical service in developing countries also present with complains of daytime sleepiness and sleep abnormalities. A large proportion of them might have Sleep Related Breathing Disorders (SRBD) and as such, it is underestimated. Within this background we conducted a study to explore the presence of SRBD among patients presenting with symptom complex of respiratory diseases in Routine Respiratory Clinical Service by use of Epworth Sleepiness Scale (ESS).

Material and Methods

A cross-sectional study of 50 patients with respiratory symptom complex was conducted in respiratory clinical service of Division of Pulmonary, Critical Care and Sleep Medicine at B. P. Koirala Institute of Health Sciences (BPKIHS) from 2014-2015. Targeted Comprehensive Sleep History and Epworth Sleepiness Scale (ESS) were used to recognize the presence of SRBD among these patients.

Results

74% patients had ESS score ≥10. Mean ESS was 12.32 (±4.76). 72% subjects had daytime fatigue, 62% loud snoring, 58% daytime sleepiness and 46% sleep fragmentation. ESS ≥10 reflected excessive daytime sleepiness (sensitivity 86.67%; 95% CI, 69.28 – 96.24; specificity 45%, 95% CI, 23.06 – 68.47; PPV 70.27%, 95% CI, 53.02 – 84.13; NPV 69.23%, 95% CI, 38.57 – 90.91).

Conclusion

Epworth Sleepiness Scale has utility in predicting SRBD in patients with respiratory symptom complex with high overall predictive accuracy. It can be used in routine clinical care to identify and predict patients having Sleep Related Breathing Disorder and refer them to clinical sleep services for further evaluation.

Key words:

Epworth Sleepiness Scale, Respiratory Diseases, Sleep Related Breathing Disorder.

Introduction

Respiratory clinics in the developing countries are burdened with myriad presentations of common conditions such as Bronchial Asthma, Chronic Obstructive Pulmonary Disease (COPD), Bronchiectasis and Interstitial Lung Diseases. With the ageing process comes the predisposition to disorders of sleep such as sleep-related breathing disorders (SRBD) and sleep disturbances such as loud snoring, excessive daytime sleepiness, daytime

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fatigue, morning headaches, and nocturnal oxygen desaturations [1]. There is a high prevalence of sleep disorders in subjects with chronic respiratory illnesses [2]. Respiratory comorbidities may mask the common manifestations of sleep disorders, leading to underestimation of its burden in subjects with respiratory diseases, that may cause poorer quality of life and outcomes despite adequate treatment of the chronic respiratory condition [3,4,5,6].

There is scarcity of data on the burden of SRBD in the Nepalese population with respiratory symptom complex, and with the polysomnography test not being readily available, a need to screen sleep disorders in this group of patients is imperative. The Epworth Sleepiness Scale for measuring daytime sleepiness correlated well with results of overnight polysomnography [7,8] and has been used a screening tool for excess daytime sleepiness.

Within this background, the study aimed to explore the presence of SRBD among patients with symptom complex of respiratory diseases in routine respiratory clinical service by use of Epworth Sleepiness Scale.

Materials and Methods

This hospital based cross-sectional study was conducted in the Division of Pulmonary, Critical Care and Sleep Medicine at the Department of Internal Medicine of B. P. Koirala Institute of Health Sciences, a tertiary care university hospital in Eastern Nepal, from May 1, 2014 to September 30, 2015. The Institute's Ethical Review Board approved the study.

Case Definitions:

Respiratory Symptom Complex: A subject was considered to have Respiratory Symptom Complex when there were cardinal manifestations of respiratory disease of a chronic duration, specifically cough with or without expectoration, dyspnea, chest pain, and/or hemoptysis of 3 or more weeks.

Sleep-Related Breathing Disorder (SRBD): SRBD was defined as repetitive episodes of apnea or hypopnea during sleep associated with sleep fragmentation, arousals and oxygen desaturation as documented by portable Apnea Link TM polysomnogram and descriptively defined based on the American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated Events (version 2.0.2) [9]. For the purpose of the study, SRBD was defined as an Apnea-Hypopnea Index (AHI) of at least 5 events per hour of sleep.

Apnea: Cessation of airflow for 10 seconds or longer during sleep, as documented by polysomnography.

Hypopnea: Decrements in airflow during sleep, and if desaturation occurred, as document by polysomnography.

Desaturation: A fall of 4% or more oxygen saturation from baseline as observed by polysomnography.

Inclusion and Exclusion Criteria: Patients aged at least 18 years, giving informed and written consent, meeting the case definitions of respiratory symptom complex and willing to undergo overnight polysomnography, were included in the study. Subjects with respiratory symptom complex who were in respiratory failure, in need of supplemental oxygen therapy, hemodynamic instability or requiring intensive care support were excluded from the study.

Recruitment of the Patients and Procedure: An informed verbal and written consent was taken. 50 consecutive patients presenting to the routine respiratory clinical service of the Division of Pulmonary, Critical Care and Sleep Medicine, meeting the inclusion criteria were recruited.

A structured proforma gathered data on Targeted Comprehensive Sleep History that included Epworth Sleepiness Scale (ESS), referenced from Johns MW (Sleep 1991)

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[7] and questions related to sleep disturbance abnormalities, such as presence of loud snoring, snorting, daytime somnolence, excess daytime sleepiness and morning headache. The Epworth Sleepiness Scale score was based on eight situational and structured short questions pertaining to sleepiness related activities of daily living, with a score of 10 or more reflecting increase probability of excess daytime sleepiness.

Results of the overnight polysomnogram, which was conducted at sleep laboratory using the ResMed ApneaLinkTM polysomnogram (portable) were recorded. Outpatients were admitted directly to the Sleep Room and inpatients were transferred to the room at time of start of sleep study. The Res Med ApneaLink® software was used to automatically analyze and derive Apnea-Hypopnea Index (AHI). The polysomnography study was started at 10:00 pm. The device monitored nasal airflow by nasal pressure transducer, respiratory efforts, chest movements and pulse oximetry. The doctor on duty was trained on the operation of the polysomnograph and mandated to monitor for any mechanical errors and difficulties faced by the subject during the session. The device was promptly stopped after a minimum of 7 hours of sleep time, or at 7:00am, whichever was earlier.

During the enrollment of subjects and the study period, standard clinical care and treatment of the subjects' respiratory symptom complex was provided as per the Institute's protocol.

Data and Statistical Analysis:

The collected data were entered in Microsoft Excel 2007 worksheet and statistically analyzed using the SPSS software version 11.5. Descriptive statistical data were presented as Mean, Standard Deviation, and percentage and proportions. For inferential statistics chi square test with risk ratio were calculated with a confidence interval of 95%, and a p value of <0.05 inferring statistical significance. For the diagnostic accuracy test of the Epworth Sleepiness Scale, tests for sensitivity, specificity; positive and negative predictive values were carried out.

Results

Of the 50 subjects with respiratory symptom complex presenting to the routine respiratory clinical services of the hospital, the sleep related abnormality questionnaires and the Epworth Sleepiness Scale answered by them showed that 74% subjects had an Epworth Sleepiness Scale score of at least 10. The mean Epworth Sleepiness Scale score was 12.32 ($\pm$4.76). The distribution of the Epworth Sleepiness Scale scores is depicted in table 1.

Table 1. Epworth Sleepiness Scale score in patients with respiratory symptom complex attending routine respiratory clinical service

Epworth Sleepiness Scale (ESS) Score	Number	Frequency %
≥ 10	37	74
<10	13	26

The study observed that many subjects (72%) suffered daytime fatigue attributed to inadequate sleep. 62% of the subjects' partners reported loud snoring; 58% had daytime sleepiness, 46% revealed feelings of restlessness and sleep fragmentation, 24% complained of morning headache, and that 18% of the patients reported having choking or gasping sensation during sleep. The presence of loud snoring in the targeted comprehensive sleep history was significantly associated with SRBD (p value <0.001), and that such subjects were at high risk of development of sleep related breathing disorder (OR 8.582, p value = 0.006, 95% CI 1.842–39.989). sleep related disturbances are depicted in table 2.

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Table 2. Sleep related disturbances in patients with respiratory symptom complex attending routine respiratory clinical service

Sleep Related Disturbances	Number	Frequency %
Loud Snoring	31	62.0
Daytime Sleepiness	29	58.0
Restlessness in sleep and sleep fragmentation	23	46.0
Morning headache	12	24.0
Choking/gasping in sleep	9	18.0

In the study, an Epworth Sleepiness Scale Score cut-off value of 10 reflected excessive daytime sleepiness with a sensitivity of 86.67% and a specificity of 45.00% for detecting the presence of Sleep Related Breathing Disorder in patients presenting with respiratory symptom complex. The utility of Epworth Sleepiness Scale Score in screening for SRBD in such patients is depicted in table 3.

Table 3. Utility of Epworth Sleepiness Scale score in screening for sleep related breathing disorders (SRBD) in patients with respiratory symptom complex attending routine respiratory clinical service

ESS Score Cut-off	AHI ≥5 (Mild-Severe SRBD)				
	PPV (95% CI)	NPV (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	AUC
≥10	70.27 % (53.02 – 84.13)	69.23 % (38.57 – 90.91)	86.67% (69.28 – 96.24)	45.00% (23.06 – 68.47)	0.66 (0.51 – 0.86)

Discussion

The study has dealt with the issue of screening for sleep disturbances and sleep related breathing disorders (SRBD) in patients with symptom complex of respiratory diseases presenting to routine respiratory clinical service in a tertiary hospital in eastern Nepal. For this purpose, the Epworth Sleepiness Scale (ESS), a targeted comprehensive sleep history using a sleep disturbance-related questionnaire, and Polysomnography were used to identify presence of sleep related breathing disorder in patients presenting with respiratory symptom complexes.

While most studies available have dealt with the screening of sleep disorders in particular respiratory disorders such as chronic obstructive pulmonary disease or bronchial asthma or the Overlap Syndrome, the present study includes all patients with a respiratory symptom complex.

About a third of the patients visiting health care facilities in developing countries complain of respiratory symptoms, with 28% Nepalese population having respiratory symptoms, [10] and more than 50% of the population suffer from some sleep disturbance, the prevalence of sleep related breathing disorders (SRBD) could be higher. In routine respiratory clinical services in Nepal, sleep disorders are uncommon diagnoses since seldom do such patients present with a sleep related problem. In fact, unmasking sleep related abnormalities from the myriad respiratory manifestations are a clinical challenge.

Daytime fatigue was the most predominant sleep disturbance seen in our study population followed by loud snoring. In fact, patients with respiratory disease who also had problem of loud snoring were at higher risk for development of sleep related breathing disorder (OR 8.582, p value = 0.006, 95% CI 1.842 – 39.989).

The Epworth Sleepiness Scale (ESS) [7] tool is a validated self-answered questionnaire that screens for excessive daytime sleepiness. In a study of the usefulness of the ESS in 50 patients with Chronic Obstructive Pulmonary Disease (COPD), most patients (76.92%) had a normal AHI and ESS score of ≤10, and only 4.17% with high AHI had ESS score

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of >10, concluding that ESS has no utility as a screening tool in COPD patients with sleep disorders [11]. In the present study, ESS was found to be a very useful instrument to search out those at risk for sleep related breathing disorder. An ESS score of ≥10 in the present study had a sensitivity of 86.67% and specificity of 45% for reflecting sleep-related breathing disorder with an AHI of ≥5 events/hour of sleep, with a positive predictive value of 70.27% (95% CI 53.02 – 84.13) and a negative predictive value of 69.23% (95% CI 38.57 – 90.91). The study results point that patients with symptom complex of respiratory disease who have high ESS scores, and who have sleep disturbance abnormalities, particularly daytime fatigue and loud snoring, may likely have coexistent sleep related breathing disorders (SRBD), and such patients need to be investigated with detailed sleep studies.

The study does have limitations in that it does not use a Class 1 polysomnograph, which would have higher accuracy in diagnosis of sleep related breathing disorders, but limitation of such resources is unavoidable in developing countries.

Conclusion

The study concludes that the Epworth Sleepiness Scale has good utility in predicting the presence of sleep related breathing disorder in patients with symptom complex of respiratory disease who visit the routine respiratory clinical services with high predictive accuracy and conducting a simple self-answered sleep disturbance abnormality questionnaire as an adjunct to the ESS strengthens the probability of presence of SRBD in such patients. The Epworth Sleepiness Scale can be used in routine respiratory clinical care to predict presence of sleep related breathing disorder and refer them to clinical sleep services for further evaluation.

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Original Article

Study of the Potential Use of Lithium in Treatment of Acute Kidney Injury in Rat Model

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Abstract

Background:

Management of acute kidney injury is still facing a big problem. It is only dependent up till now on supportive measures, like fluid resuscitation and renal replacement therapy. No current drug therapy has been approved for the treatment of acute kidney injury. Acute kidney injury situations in a lot of cases can be predicted so, finding a drug for AKI will really benefit many patients. The pathophysiology of AKI is complex and many signaling pathways are involved in it. The Glycogen synthase kinase 3B enzyme is an important member in some of these pathways. The effect of its inhibition by the FDA approved drug, lithium on AKI is still under study.

Material & Methods

The current study was conducted on28 Male Sprague–Dawley rats. We classified the rats into groups. We induced acute kidney injury to rats with cisplatin. We administered lithium chloride to treat AKI in comparison with saline treatment. We have done renal functions and histopathological examinations to all rats enrolled in our study.

Results

Single intraperitoneal injection of cisplatin (5 mg/kg) in rat induced acute kidney injury. The effect of lithium chloride treatment with dose (80 mg/kg) on serum creatinine and blood urea levels showed significant regression in the rising of serum creatinine and blood urea in lithium chloride treated rats in comparison to saline-treated rats. Pathological pictures and scores demonstrated an improvement in lithium chloride treated rats than saline-treated but results were not significant.

Conclusion

Administration of lithium may be a promising treatment for acute kidney injury.

Key words:

Acute kidney injury - Lithium

Introduction

Acute kidney injury (AKI) is defined "as a clinical syndrome characterized by a rapid decrease in renal function together with the accumulation of waste products such as urea"[1]. The incidence of AKI differs from community, hospital and ICU admissions. AKI incidence is 1-7% in hospital admitted patients and 1-25% in ICU admitted patients. AKI is a serious disease which increases the mortality rate ten to fifteen times in ICU admitted

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patients [2]. Drugs and various toxic substances are eliminated through the kidney. So, the kidney is one of the important organs to be affected by drugs. Unfortunately, the incidence of drug-induced kidney disease is not exactly confirmed. Some studies demonstrated that it is 6-80% in AKI that occurs during hospital admission [1].

Management of acute kidney injury is still facing a big problem. It is only dependent up till now on supportive measures, like fluid resuscitation and renal replacement therapy. No current drug therapy has been approved for the treatment of acute kidney injury [3]. AKI is now being considered an important cause of chronic kidney disease. Failure of complete recovery from AKI transfers acute kidney injury patient to be CKD patient in 90 days [4]. The pathophysiology of AKI is complex and many signals' pathways are involved in it. The Glycogen synthase kinase 3B enzyme is an important member in some of these pathways. GSK3B enzyme is serine/threonine protein kinase responsible for regulation of the metabolism of glucose [5] the effect of its inhibition by the FDA approved drug, lithium on AKI is still under study. [6]. Many factors affect recovery from AKI from them, the condition of the kidney before the development of AKI, the general condition of the patient, the presence or absence of chronic disease in the heart, chest or liver and the age of the patient is very important factor [7].

Materials and Methods

This study was conducted on 28 Male Sprague–Dawley rats between 1stof April 2017 to 20th of May 2017. All the rats were at the age of 6-8 weeks old weighting between 150 and 250 gm at the beginning of the study. The experimental protocols were approved by the Ethics Committee of the University of Menoufia. At the start of our work rats were classified into 4 groups. First group rats were subjected to induction of AKI by cisplatin (5mg/kg) intraperitoneal injection (IP). Second group, rats were given saline same dose like cisplatin IP. The previous 2groups' blood samples were obtained and tissue samples were taken from the left kidney at day 3 from the start. Third group, rats were given lithium chloride (80mg/kg) IP at day 3. Fourth group, rats were given saline IP the same dose like lithium chloride dose at day 3. The previous 2 groups, blood samples were obtained and tissue samples were taken from the left kidney at day 5from the start. Tissue samples from the left kidney were kept in buffered 10% formalin for histopathological examination. Blood samples were obtained from the retro-orbital vein of the rat for renal functions assessment. Formalin-fixed left kidney was embedded in paraffin and was prepared in 3-micrometer–thick sections. Hematoxylin and eosin were used to stain sections to estimate gross histologic kidney injury of Tubulo interstitial injury and tubular dilation/sloughing severity was semi quantitatively scored on a scale from 0 to 5 and reported as the mean of 20 random high-power (3200) fields per hematoxylin and eosin–stained section as the following **:(5)** '0: none, 1: 10%, 2: 11%–25%, 3: 26%–45%, 4: 46%–75%, 5: 76%'. Collection, tabulation and statistical analysis of collected results were done. Analysis by an IBM compatible personal computer with SPSS statistical package version 20 (SPSS Inc. Released 2011 was done. (IBM SPSS statistics for windows, version 23.0, Armonk, NY: IBM Corp.). Two types of statistical analysis were used: Descriptive statistics and Analytic statistics.

Results

The results of our study revealed that induction of AKI was achieved by a single intraperitoneal injection of cisplatin (5 mg/kg) in rat. (Table 1) cisplatin injury

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resulted in an elevation of serum creatinine and blood urea levels by the third day. At day 3, cisplatin induced a typical pattern of (ATN), which was characterized by epithelial simplification, vacuolization of proximal tubular epithelium, epithelial necrosis, and luminalectasia, loss of brush border and slough of tubular cell into lumen (Table 2) (Figure 1).

Saline injection same dose like cisplatin did not cause any elevation in serum creatinine and blood urea levels at day 3. Histopathology of kidneys from rats treated alone with saline remained normal (Figure2).

After day 3, serum creatinine and blood urea levels in cisplatin-injured rats continued to rise. The effect of lithium chloride treatment on serum creatinine and blood urea levels showed significant regression in the rising of serum creatinine and blood urea in lithium chloride treated rats in comparison to saline-treated rats.

Serum creatinine (6.06 ± 0.72) in saline group versus (3.15 ± 1.87) in lithium chloride low dose group and 4.06± 1.99 in lithium chloride high dose group. Blood urea (407.84 ± 171.59) in saline group and (128.88 ± 76.06) in lithium chloride group which signifies an increased renal recovery from AKI with the injection of lithium chloride.

The lithium-enhanced recovery in renal function was accompanied by improved histopathologic picture and pathology scores. Pathological pictures and scores demonstrated an improvement in lithium chloride treated rats than saline-treated but results were not significant. (Figure3) (Figure4) (Table3) (Table4).

Collectively, these data suggest that lithium chloride has an obvious improving effect that enhances renal function recovery and kidney repair after Acute Kidney Injury.

Note of, the dose of lithium used in our study (80 mg/kg) is lower than the dose of lithium (120 mg/kg) that has been safely and routinely used for studies in neurobiology in rodents [8].

The figures were taken during histopathological examination of rat's kidney

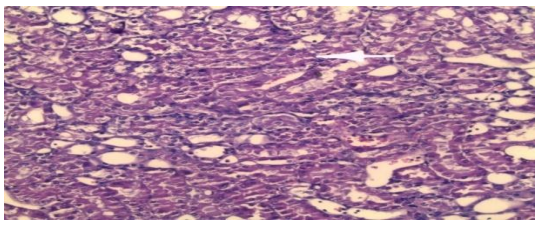

Figure (1): *Cisplatin-induced AKI day3. rat n: 7(Necrosis)*

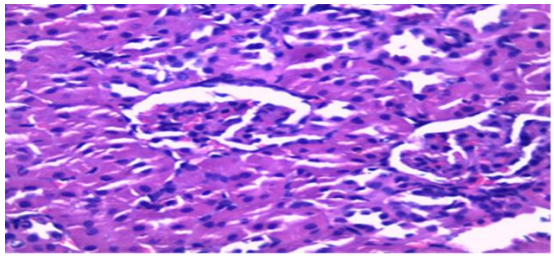

Figure (2): *Saline kidney. Day 3 Rat n: 6(no changes)*

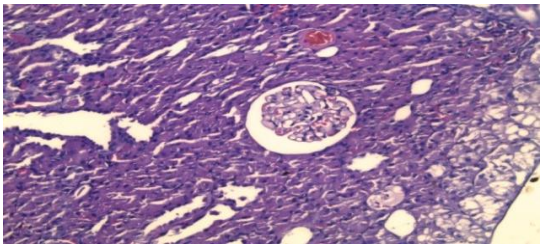

Figure (3): *Lithium chloride treated rats. Day 5: rat n: 5(Cellular vacuolization & foal loss of brush border)*

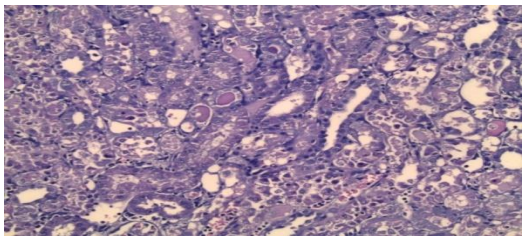

Figure (4)*: Saline treated rats. Day 5: rat n: 7(loss of brush border, sloughing, Focal vacuolization and epithelial death)*

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Table1: comparison between day3 renal functions of rats with cisplatin-induced AKI (GroupI) and saline-injected rats (GroupII)

	Group I (n = 7) Mean ± SD	**Group II (n = 7) Mean ± SD**	**Mann Whitney test**	**P value**
Blood Urea (mg/dl)	132.63 ± 44.73	64.97 ± 7.99	3.13	0.002
Serum Creatinine (mg/dl)	0.70 ± 0.26	0.41 ± 0.06	2.82	0.005

This table demonstrates that Blood urea and serum creatinine were significantly higher in group I than group II.This means that induction of AKI was achieved by a single intraperitoneal injection of cisplatin (5 mg/kg) in rat.
SD: standard deviation

Table2: comparison between day3 pathology scores of rats with cisplatin-induced AKI (GroupI) and saline-injected rats (GroupII)

	Group I (n = 7) Mean ± SD	**Group II (n = 7) Mean ± SD**	**Mann Whitney test**	**P value**
Pathology score	3.14 ± 1.34	0.14 ± 0.37	3.28	0.001
	No. %	No.%	Z test	P value
Pathology score 0 1 2 3 5	0 0.0 0 0.0 3 42.9 2 28.6 2 28.6	6 85.7 1 14.3 0 0.0 0 0.0 0 0.0	2.7 0.00 1.30 0.76 0.76	0.006 0.99 0.19 0.44 0.44

This table demonstrates that the mean pathology score was significantly higher in group I (cisplatin-induced AKI group) than group II (saline-injected rats).
SD: standard deviation

Table3: comparison between day5 renal functions between cisplatin induced AKI rats that were treated with lithium chloride in day 3(GroupIII) and were treated with saline in day3 (GroupIV)

	Group III (n = 6) Mean ± SD	**Group IV (n = 6) Mean ± SD**	**Mann Whitney test**	**P value**
Blood Urea (mg/dl)	128.88 ± 76.06	407.84 ± 171.59	2.55	0.01
Serum Creatinine (mg/dl)	4.06 ± 1.99	6.06 ± 0.72	2.19	0.02

This table demonstrates that lithium chloride treated rats (GroupIII) shows significant reduction in renal functions than saline-treated rats (GroupIV)
SD: standard deviation

Table4: comparison between day5 pathology scores between cisplatin-induced AKI rats that were treated with lithium chloride in day 3(GroupIII) and rats that were treated with saline in day3 (GroupIV)

	GroupIII (n = 7) Mean ± SD	**GroupIV (n = 7) Mean ± SD**	**Mann Whitney test**	**P value**
Pathology score	2.42 ± 1.27	2.57 ± 0.78	0.33	0.73
	No. %	No.%	Z test	P value
Pathology score 1 2 3 4	2 28.6 2 28.6 1 14.3 2 28.6	0 0.0 4 57.1 2 28.6 1 14.3	0.76 0.54 0.00 0.00	0.44 0.59 0.99 0.99

This table demonstrates that lithium chloride treated rats (GroupIII) shows improvement in pathology scores than saline-treated rats (Group IV)
SD: standard deviation

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Discussion

Lithium is one of the important inhibitors of the GSK3B enzyme. It has a regenerative effect on various body tissues. Involving tissues of the central nervous system and tissues in bone marrow forming hematologic system. Kidney tissues is emerging now to benefit from the regenerative effect of lithium but this is still under research [5].

In agreement with our results: Plotnikov and coworkers 2016 [9], in their preclinical animal study, founded that inhibition of GSK-3b activity through pharmacological treatment by lithium chloride resulted in significant decrease of AKI. Wangand Tong 2015 [10], in their preclinical animal study on rats, demonstrated that glycogen synthase kinase-3B inhibition by TDZD-8 provided a protection to the kidney. Bao and coworkers2014 [5], in their preclinical animal study examined the effect of administration of lithium on cisplatin and ischemia/reperfusion-induced AKI. Their results are in consistent with our study results.

Plotnikov and coworkers 2013[11], in their preclinical animal study demonstrated that LiCl treatment reduced renal tubular cell death and reduced kidney injury caused by gentamicin. Bao and coworkers 2012 [12], in their preclinical animal study, suggested that the inhibition of GSK3β by new selective small molecule inhibitors or existing FDA approved drugs with GSK3β inhibitory function, like lithium and valproate, represents a new therapeutic strategy for AKI treatment, especially for NSAID-induced AKI. The results of the previous study are in consistent with our study results.

Howard and coworkers 2012[13] in their preclinical animal study on mice clearly demonstrates the essential role of GSK-3β in AKI development so, its inhibition according to these results really is beneficial in treating AKI. Wang and coworkers 2010 [14] in their study demonstrated that activation of GSK3β-mediated Bax activation induced apoptosis and tubular damage. Therefore, its inhibition will improve AKI through this pathway.

Our study was carried out on 42 Male Sprague–Dawley rats aged 6-8 weeks old weighted between 150 and 250 gm. Rats were classified into 4 groups. Group I: rats were subjected to induction of AKI by cisplatin (5mg/kg) intraperitoneal injection(IP). Group II: rats were given saline same dose like cisplatin IP. The previous 2 groups' blood samples were obtained and tissue samples were taken from the left kidney at day 3 from the start. Group III: rats were given lithium chloride (80mg/kg) IP at day 3. Group IV: rats were given saline IP the same dose like lithium chloride dose at day 3. The previous 2 groups, blood samples were obtained and tissue samples were taken from the left kidney at day 5 from the start. Our study results revealed that cisplatin (5mg/kg) induce AKI. Lithium chloride promotes renal recovery after its administration for treatment of acute kidney injury.

Conclusion

Administration of lithium, the FDA approved drug as one of the glycogen synthase kinase 3B inhibitors may be a promising treatment for acute kidney injury.

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Original Article

Outcome of Patients with Gullain Barre syndrome at Tertiary Care Hospital in Eastern Nepal.

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Abstract

Background

Gullain Barre syndrome is the most common cause of acute flaccid paralysis. Early diagnosis and treatment improves survival in patients with Gullain Barre Syndrome.

Material and Methods

The purpose of the study was to note the common clinical features and identify predictors of outcome in Patients with Gullain Barre Syndrome. It is a prospective study which was conducted at Nobel Medical College Teaching Hospital from April 2015 to March 2016.

Results

Time between onset of symptoms, presentation to hospital and admission was 5 ± 4 days. Four Patients (20%) gave history of upper respiratory tract infections and 12 (60%) had diarrhoea. Limb weakness was the most common symptom, which was documented in 20 (100%) patients. Other common symptoms were limb paresthesia, limb pain, and bladder dysfunction. Cerebrospinal Fluid protein was raised in 16(80%) patients to more than 45 mg/dl. All of our patients had CSF cell count less than 10. One (5%) patient had normal nerve conduction study initially. Eight (40%) patients had axonal (AMAN) variant of GBS, 3(15%) had AMSAN variant of GBS, while 8(40%) had demyelinating neuropathy (AIDP). The mean duration of hospital stay was7.4 ±2.7 days. Three months after hospital discharge 12(60%) patients achieved complete recovery. Eight (40%) patients still needed some support with ambulation. Predictors of worse outcome were old age, rapid progression of disease and AMSAN variant of GBS.

Conclusion

Gullain Barre syndrome is an important cause of acute flaccid paralysis in children and adults. Early diagnosis is based on history of symmetrical limb weakness, CSF Findings and nerve conduction study. Majority of patients improve with supportive care while some develop respiratory failure and needs mechanical intubation.

Key Words

AIDP, AMAN, Gullain Barre Syndrome, IVIG, Plasmaphresis

Introduction

Guillain-Barré syndrome is an important cause of acute peripheral neuropathy that manifests clinically with limb weakness and may progress for up to 4 weeks. The pathogenesis of disease involves either inflammatory demyelination or axonal degeneration. Gullain Barre Syndrome has been reported from all over the world. Guillain-Barré syndrome is more common in men. Epidemics of Guillain-Barré syndrome is noted in summer in Northern China with

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association with C. jejuni infection [1]. A few weeks before the onset of Guillain-Barré syndrome majority of patients report nonspecific infections of upper respiratory tract or diarrhea. Guillain-Barré syndrome may also be triggered by trauma, vaccination or surgery [2]. The affected nerves show Multifocal segmental demyelization [3]. Several variants of Guillain-Barré syndrome have been reported which include acute inflammatory demyelinating poly radiculo neuropathy, acute motor-sensory axonal neuropathy and acute motor axonal neuropathy and Miller Fisher syndrome [4,5].

Most of the patients with Guillain-Barré syndrome improve over weeks or months. Nearly 3 to 8% of patients die due to complications like pulmonary embolism, sepsis. Permanent disabling weakness, imbalance, or sensory loss occurs in 5 to 10 percent [6]. This study was undertaken to determine which variant of GBS was common in the Eastern part of Nepal and to identify the prognostic factors.

Material and Methods

The study was conducted at Nobel Medical College, Nepal. All the patients who were admitted with diagnosis of Gullain Barre Syndrome between June 2016 and May 2017 were enrolled in the study. It is a prospective study which was conducted at Nobel Medical College Teaching Hospital from April 2015 to March 2016. Detailed information was obtained from each patient regarding age, sex, clinical feature, disability, preceding illness. The diagnosis of acute Guillain-Barré syndrome was based on the finding of symmetrical ascending limb weakness with hypo or areflexia and Cerebrospinal fluid showing albumin cytological dissociation. The patients were examined during the hospital stay and were followed up until 3 months after discharge from hospital. Data were entered into the Microsoft Excel and analyzed using SPSS 17.

Nerve conduction was performed soon after admission to hospital. The patients were classified into demyelinating or axonal variant of Guillain-Barré syndrome based on electrophysiological studies [8]. The disability of the patients was graded based on the functional grading scale of Hughes *et al*. [9]

Scale of Hughes

Grade 0	Normal functional state
Grade 1	Able to run with minor signs and symptoms
Grade 2	Able to walk 5 m independently
Grade 3	Able to walk 5 m with aid
Grade 4	Bed- or chair-bound
Grade 5	Requires assisted ventilation

Results

Clinical features and laboratory parameter of the patients

Table 1. Demographic profile of the patients

Clinical characteristics	Number of patients(N = 20)
Age in years	31.7 ± 15.5
Sex Male Female	 12.0(60%) 8.0(40%)
Preceding infection Upper respiratory infection Diarrhoea	 4.0(20%) 12.060%)
Time of onset of symptoms and presentation to hospital (in Days)	5.0

Most of our study patients were young with male predominance. Eighty percent of our study patients had infection prior to onset of the illness.

Table 2. Clinical characteristics of the patients

Characteristics	Number of patients(N)
Limb weakness	20(100%)
Sensory symptoms	12(60%)
Facial diplegia	6(30%)
Absent deep tendon reflexes	20(100%)
Autonomic dysfunction	7(35%)
Numbness	8(40%)
Shortness of breath	6(30%)

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All the patients who presented to hospital had limb weakness and absent deep tendon reflexes. Thirty percent of patients had respiratory problem with need for respiratory support.

Table 3. Investigation findings of the patients

Characteristics	Number of patients(N)
CSF Cell Count	
Normal	19(95%)
Raised	1(5%)
CSF Protein	
Normal	4(20%)
Raised	16(80%)

Majority of our study patients had normal cell count. Cerebrospinal fluid Protein was raised in 80% of patients.

Table 4. Treatment offered to the patient

Characteristic	Number of patients(N)
Supportive care	20(100%)
IVIG	1(5%)
Plasmaphresis	0
Mechanical ventilation	1(5%)
Length of hospital stay	7.4±2.7
Prognosis	
Complete recovery	8(40%)
Residual deficit	12(60%)
Death	0

All of our patients were given supportive care. One patient needed mechanical ventilation that was provided intravenous immunoglobin. Duration between onset of symptoms and admission to hospital was 5 ± 4 day. Eleven (55%) patients did not report any infection or event preceding the onset of illness. Four (20%) patients gave history of upper respiratory infections and 12 (60%) patients reported having diarrhea prior to onset of GBS. Limb weakness, was documented in 20 (100%) patients. Limb paresthesia, limb pain, and facial weakness were reported by some patients. In all the patients CSF analysis was done after the first week which increased the probability of having higher CSF protein. CSF protein was raised in 16(80%) patients to more than 45 mg/dl. One patient had CSF protein higher than 100 mg/dl. All of our patients had CSF cell count less than 10. Nerve conduction study was done soon after hospital admission. One (5%) patient had normal study initially. Eight (40%) patients had axonal(AMAN) variant of GBS,3(15%) had AMSAN variant of GBS, while 8(40%) had demyelinating neuropathy(AIDP).

The mean duration of hospital stays was7.4 ±2.7 days. One patient (5%) required mechanical ventilation. Most of our patients were managed with supportive care. Five percent of our patients received intravenous immunoglobin. Patients were assessed for their disability at the time of discharge from hospital and after 3 months. Three months after hospital discharge 12(60%) patients achieved complete recovery. Eight (40%) patients still needed some support with ambulation.

Discussion

Guillain Barre Syndrome is an important cause of acute flaccid paralysis. Acute inflammatory demyelinating neuropathy is the most common variant of Guillain-Barré syndrome in the western world while in China acute motor axonal neuropathy variant of GBS is the commonest. In our study ,12(60%)of our patients had acute axonal variant of GBS while only 8(40%) had demyelinating variant of GBS. All of our patients who got admission to the hospital had limb weakness. Twelve (60%) of our patients needed some support for ambulation. Eight (40%) of the patients were ambulant at hospital admission and were discharged from hospital after few days of observation once their weakness remained static and showed some signs of improvement. Majority of our patients also had sensory symptoms in the form of paresthesia, tingling (60%). Some had autonomic dysfunction in the form of

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resting tachycardia, hypotension, and hypertension (35%).

In our study 5(25%) patients had history of diarrhea while 4(20%) had history of upper respiratory infection 2-3 weeks preceding the illness. Most patients with Guillain–Barré syndrome experience signs and symptoms of an infection like upper respiratory tract illness or diarrhea prior to the onset of the neurological symptoms [10]. In the present study lumbar puncture was performed at second week of the onset of limb weakness as the cerebrospinal fluid profile may be normal during the first week of illness. Elevated cerebrospinal fluid protein concentration in Guillain-Barré syndrome is due to increased blood–CSF barrier permeability [11, 12]. In the present study, (80%) patients showed albumin cytological dissociation on CSF examination. Elevated cerebrospinal protein levels are found in approximately 50% of patients in the first 3 days after onset of weakness, which increases to 80% after the first week [13]. Predictors of worse outcome in terms of severe disability and longer duration of hospital stay were older age of onset, rapid progression of disease and AMSAN variant of GBS.

All the patients who got admission to the hospital received supportive care. These included physical therapy, change of body position, measures to prevent aspiration pneumonia, deep vein thrombosis, fluid and nutritional support. Patients with Gullain Barre syndrome need careful and regular monitoring of respiratory function and autonomic dysfunction, such as heart rate, arrhythmia, and blood pressure [14]. Infections need to be prevented [15]. Deep-vein thrombosis, various symptoms of autonomic dysfunction have to be identified and treated early. Identification and management of pain, physiotherapy, and rehabilitation is important [16]. Psychosocial care is also reported to be important [17, 18]. Only one patient received intravenous immunoglobin.

Conclusion

Patients with Gullain Barre syndrome were diagnosed on the basis of symmetrical limb weakness and areflexia. Advanced age of onset, rapid progression of the illness and need for mechanical ventilation was found to be associated with worse outcome. Majority of patients improve with supportive care while some develop respiratory failure and needs mechanical intubation.

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Original Article

Age distribution of patients presenting with typhoid and paratyphoid fever in Kathmandu, Nepal

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Abstract

Background

Enteric fever is a significant cause of morbidity in Nepal. In the past, *Salmonella enterica*serovar Typhi (*S.* Typhi) was the major causative organism of enteric fever. However, more recently, *Salmonella enterica*serovar Paratyphi (*S.*Paratyphi) A has been isolated from most patients presenting with enteric fever in various regions of Nepal. This study aimed to evaluate age differences in patients presenting with typhoid and paratyphoid fever.

Materials & Methods

Between December 2014 and October 2015, 186 patients presented with enteric fever to the Civil Service Hospital in Kathmandu. *S.* Typhi and *S.*Paratyphi A were isolated from blood cultures in 48.4% and 51.6% of the cases, respectively. Age groups of the patients infected with either serovar were compared.

Results

The mean age of patients from whom *S.* Typhi was isolated was 19.3 years, while the mean age of patients from whom *S.* Paratyphi A was isolated was 25.2 years; p=0.025.

Conclusion

Our study shows that age is an important factor in having either typhoid or paratyphoid fever. This will help in the prevention of typhoid and paratyphoid fever in various age groups.

Key words

S. Typhi, S. Paratyphi A

Introduction

Enteric fever is a significant cause of morbidity and mortality worldwide [1]. Typhoid fever and paratyphoid fever fall under the umbrella of enteric fever, caused by the bacteria *Salmonella enterica* serovar Typhi *(S*. Typhi) and *Salmonella enterica* serovar Paratyphi (*S*. Paratyphi) A, B and C [2]. It is estimated that in the year 2000 alone, typhoid fever caused over 21.6 million illnesses and over 200,000 deaths worldwide [1]. In the same year, it was estimated that there were over 5 million illnesses of paratyphoid fever. The incidence of typhoid fever was the highest in south-east Asia and south-central Asia at above 100/100,000 cases per year [1]. These findings are comparable to a systematic review conducted in 2010 which reported an estimated 26.9 million typhoid fever cases that year [3]. While *S.* Typhi is reported to be the more common

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cause of enteric fever, *S.* Paratyphi A has also emerged as a significant cause of illness in Asia [4].

Enteric fever thrives in overcrowded and unsanitary environments across the developing world [5]. *Salmonella* spp. are shed in urine and faeces and are mainly transmitted through ingestion of contaminated food or water [5]. In less industrialized countries such as Nepal, where unsafe drinking water, inadequate disposal of sewage, and flooding are common, these organisms are transmitted through the ingestion of contaminated water [6]. *S.* Typhi and *S.* Paratyphi A cause systemic infections and upon the onset of bacteremia, patients present to the hospital with fever and malaise [5]. In Nepal, *Salmonella* infection is a common cause of fever. In this study, the rates of *S*. Typhi and *S*. Paratyphi A infections in Kathmandu are compared, and the age distribution of patients infected with either serovar is evaluated.

Materials & Methods

The Widal agglutination test continues to be a popular method for detection of typhoid fever; however, it has low specificity and sensitivity [7]. Isolation of the organism provides more accurate detection and remains the gold standard for diagnosis of enteric fever [7,8]. The Civil Service Hospital in Kathmandu is one of the few locations in Nepal where affordable culture facilities are available for the diagnosis of bacterial infections. The isolation of specific *Salmonella* spp. from blood cultures provides a clearer picture of the prevalence of typhoid and paratyphoid fever in the community. Furthermore, easy and affordable access to medical services at this location attracts many patients from various ethnic and economic backgrounds. As such, patients presenting to this facility are representative of the general Nepalese population.

Between December 16, 2014 and October 17, 2015 (Poush, 2071 to Ashwin, 2072) 5151 blood samples were collected and cultured at the Civil Service Hospital. Microbial growth was first detected using the automated BACTEC™ FX blood culture system. Positive samples were then cultured in MacConkey agar and blood agar for detection of specific bacteria. For the purpose of this study, 186 culture positive cases of *S.* Typhi and *S.* Paratyphi A were retrospectively evaluated. All medical data were obtained from the electronic medical records software, MiDAS. Data analysis was performed with Excel 2013 for Windows and IBM SPSS Statistics 20 for Windows. Student's t test was used to obtain the mean ages, standard deviations and the significance of the difference in the mean ages between the *S*. Typhi group and the *S*. Paratyphi A group. The level of significance was $p = 0.025$.

Results

Among the 5151 total blood samples that were cultured in 10 months, there were 186 positive cases of enteric fever (3.6%). *S.* Typhi was isolated from 90 patients (48.4%) and *S*. Paratyphi A was isolated from 96 patients (51.6%). The male to female ratio was 1.4:1 and 1.7:1 for *S.* Typhi and *S.* Paratyphi A, respectively. The mean age of patients from whom *S.* Typhi was isolated was 19.3 years (SD = 9.0), while the mean age of patients from whom *S.* Paratyphi A was isolated was 25.2 years (SD = 12.6). This difference was significant with a p value of 0.025. The 95% confidence interval was 17.4 – 21.2 years and 22.8 – 28.0 years for the S. Typhi and S. Paratyphi A groups, respectively. As shown in figure 1, the frequency of *S.* Typhiwas higher in the younger age groups while the frequency of *S.*Paratyphi A was higher in the older age groups.

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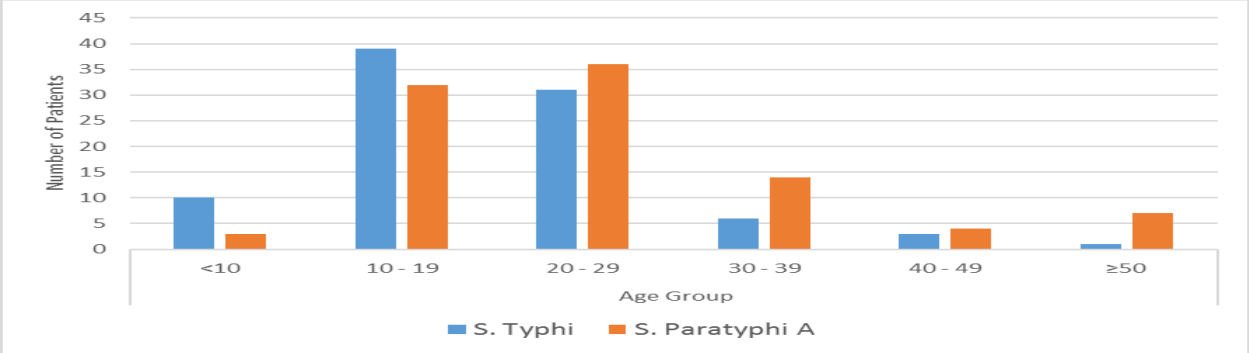

Figure 1. Age distribution of patients infected with S. Typhi versus S. Paratyphi A.

Discussion

S. Typhi has an earlier evolutionary history and has been the more common causative agent of enteric fever in the past [8,9]. However, recent evidence suggests that *S.* Paratyphi A has emerged as a significant cause of enteric fever in Asia [4]. In fact, in south-east China *S.* Paratyphi A is the major causative agent, surpassing *S.* Typhi. *S.*Paratyphi A accounts for a significant proportion of enteric fever cases in India and Pakistan as well [4]. Furthermore, this serovar was isolated from over half of the patients presenting with enteric fever to hospitals in Chitwan and Kathmandu [10,11]. Similarly, in this study, *S.* paratyphi A was the causative organism in 51.6% of the enteric fever cases, corroborating the emerging threat of this organism across south-east Asia. Both typhoid and paratyphoid fever were more common in males than in females. This finding is consistent with other studies performed in Nepal [12,13].

This study demonstrates a significant difference in the mean ages of typhoid patients when compared to paratyphoid patients. Typhoid fever was associated with younger age, while paratyphoid fever was associated with older age. The association of typhoid fever with young age has been validated by numerous national and international studies [12-14]. Immunity against *S.* Typhi lasts approximately one year after the onset of illness in non-endemic areas [15]. However, there is evidence to suggest lifelong immunity in endemic areas where the host receives persistent booster stimulations of *S.* Typhi bacilli from the environment [15]. *S.* Typhi is endemic in Nepal and many adults have suffered from typhoid fever in childhood. As such, it is possible that adults who recovered from *S.* Typhi infections in childhood, and are living in this endemic area, have acquired lifelong immunity against this serovar, resulting in a decreased frequency of typhoid fever in the older population.

With *S.*Paratyphi A becoming increasingly more common in Asia, it is possible that previously unexposed adults are now being exposed to and suffering from paratyphoid infections. *S.* Typhi specific vaccines provide little, if any cross protection against *S.*Paratyphi A [9]. Therefore, it is safe to assume the same is true after natural infection with *S.* Typhi. This may explain the higher number of paratyphoid cases in the older age groups. Other literature also states that paratyphoid fever is more frequently observed in adults [4].

Evidence from Indonesia shows that risk factors for typhoid fever include lack of sanitation facilities, hand-washing without soap, typhoid patients in the household, and sharing food from the same plate (i.e. factors within the household) [14]. Interestingly, paratyphoid fever seems to have different risk factors such as consumption of food from street vendors and flooding (i.e. factors outside the

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household) [14]. Such a clear distinction between the risk factors for typhoid and paratyphoid fever warrants closer investigation into age-related exposure levels to these factors. For instance, children may share food from the same plate more frequently than adults or they may be more likely to practice hand-washing without soap. Such investigations may provide a better understanding of the findings of this study. Furthermore, it will also aid in the design and implementation of effective interventions for the prevention of transmission.

Conclusion

Enteric fever continues to be an important public health concern in Nepal. While *S.* Typhi has been the major causative organism for decades, *S.* Paratyphi A has emerged as an equally significant threat. As humans are the only host of the causative organisms, elimination is possible. Further studies for the identification of age-related typhoid- and paratyphoid-specific risk factors will aid in prevention and elimination efforts.

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Original Article

The unified theory – Neurology of emotions and how to control them

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Abstract

Introduction

The major emotions such as fear, anger, joy and sadness are created through a complex mechanism in the temporal lobe combining data from all the sensory inputs to the brain. However, these emotions may turn into extreme manifestations when the hypothalamus and the autonomic nervous system transform these emotions to panic, rage, orgasm/laughter and grief. The Papez circuit which is at play for this "different turn" may be inactivated or could be over ridden by forebrain activity, that is, sequencing. This probably was the reason to the old adage of counting to ten when one is emotional. In this article, we hope to look at the basis and the neurology behind this and formulate a method to overcome panic.

Materials & Methods

A pilot study of 10 children aged 10 -16 was done on 16th October 2017. These children were shown pictures inducing fear and anger. A Visual Analogue Score (VAS) was used to determine the induced emotion. Next, the children were made to do sequencing tasks like mathematical calculations while viewing the similar graphics again. The new score was recorded and the data analyzed.

Results

The most frequently recorded VAS (n = 4) before sequencing was around 6.0, and between 3.0-3.5 post sequencing. The mean VAS without sequencing was 6.19 ± 0.91, which reduced to 3.65 ± 0.665. On comparing the individual VAS scores before and after sequencing, there was a general trend of a decreased VAS post-sequencing. The results were statistically significant with a p-value <0.05.

Conclusion

The study indicated that some form of sequencing while perceiving the fearful or any emotional stimuli might blunt the emotion and may not produce extreme emotions. This would be an extremely interesting and useful piece of information for many who are in cutting edge professions and competitive sports. However, much study needs to be performed to further validate this initial conclusion.

Key Words

Amygdala, Emotions, Fear, Inhibition (Psychology).

Introduction

Our emotions are the responses to the five senses our body perceives; and associates them with the stored memories from the past to bring about a pleasant or unpleasant behavior. A human being can experience four emotions including happiness, sadness, fear and anger. How

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these emotions can be projected upon us is the function of the limbic system, and most importantly, the amygdala, that plays a central part in acquisition of sight, hear, taste, smell and touch. The presumed role of the limbic structures connecting the hippocampal and para hippocampal region with the mammillary bodies, anterior thalamic nuclei, and the cingulated gyrus form the Papez circuit [1] The neuronal circuitry of the Papez Circuit processes all the information and relays it via the thalamus to the cortex and the hypothalamus and generates a series of changes in the hormonal and autonomic controls by the pituitary and the adrenal glands respectively. The "fight or flight" mechanism by the sympathetic stimulation is classic example of the body's response to fear.

It is not true that a particular sensory input will elicit a similar response each time and in each individual. This behavioral variability is the effect of both, the social and personal context in which a signal is perceived. For example, a girl who has been raped will recall her trauma every time she is touched, and this fear can occasionally transform into panic on being touched in a particular way. On the contrary, that similar touch might elicit a pleasant response in another girl who will associate this as a gesture of love and admiration. These differences in responses are a result of the preformed memories associated with the events, which take us back to react in accordance with our experiences from the past. The interesting fact remains that the same sensory inputs can emit different responses.

The uninhibited release of stimuli by the Papez circuit and the hypothalamus recruits continued autonomic and hormonal discharges. This results in unstoppable responses leading to extreme consequences. These, for example, if may turn happiness into ecstasy, sadness into grief, fear into panic and anger into rage. Uncontrolled "happiness" may result in early orgasm resulting in premature ejaculation. Uncontrolled "fear" can turn into panic resulting in a post-traumatic stress disorder experienced very frequently by survivors of physical or mental trauma.

The presence of a cognitive inhibitory control by the frontal lobe is essential for a flexible behavior. The fronto-basal-ganglia circuit initiates a stop signal task in the form of sequencing which is a serial order in behavior to bring about a stop to the continued discharge of autonomic responses. This can include counting numbers from 1 to 100, in forward or backward order; odds or evens; multiples and many more complex patterns. The goal is to achieve the sequencing needed to stop a behavior from being elicited too much. The more complex the sequence is, the better the control will be over inhibition of response. This mechanism is the basis of cognitive behavioral inhibition as seen in many experiments. The forebrain, and the usage of it, hence plays a crucial role in keeping a check on the levels of expressed emotions, and sequencing is one method to achieve this counter regulation.

Materials and Methods

A group of 10 children aged between 10 and 16 were asked to volunteer for the study on 16th October 2017. They were subjected to pictures & video clips that would make them angry, sad, happy or afraid. A Visual Analogue Score (VAS) was obtained on a scale of 1 to 9 and the results were charted for each participant without undergoing any form of sequencing or calculations being done at the time when the subject was visualizing the pictures. A second test was run on the same participants and this time, the Visual Analogue Score was obtained while undergoing sequencing patterns or calculations being done at the time when

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the subject was visualizing the pictures. The difference in the mean values of VAS before and after sequencing was calculated using a paired t-test keeping a 95% confidence interval.

Results

All the 10 participants were able to express emotion in response to stimulus as recorded by the VAS Scores obtained. [Figure 1] compares the frequency and the means of the obtained VAS. The most frequently recorded VAS (n=4) before sequencing was around 6.0, whereas after sequencing was between 3.0 and 3.5. The figure shows that the mean Visual Analogue score after emotional perception without sequencing was 6.19± 0.91, which significantly reduced to 3.65 ± 0.665. [Table 1] shows the results of a paired t-test in a tabular form. On comparing the individual VAS scores in each participant before and after sequencing, as in [Figure 2], we can clearly see a general trend ofa decreased VAS post-sequencing. There was a statistically significant difference between the two data sets; before and after sequencing, showing a p-value <0.05 (0.001).

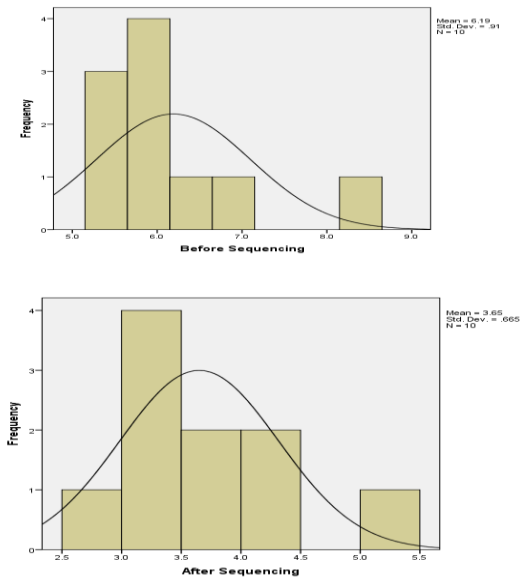

Figure 1: The frequency and mean Visual Analogue Score before & after sequencing

Table 1: Paired sample t-test to show the difference in mean and the standard deviations

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Before Sequencing	6.190	10	.9098	.2877
	After Sequencing	3.650	10	.6654	.2104

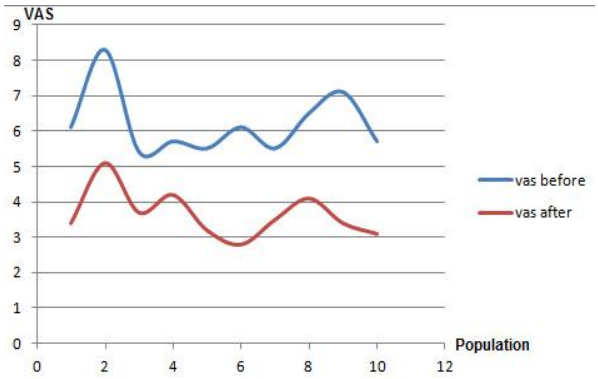

Figure 2: Difference between the individual Visual Analogue Scores before and after sequencing.

Discussion

It is quite often that many people find themselves in a situation of the red haze, panic, overwhelming impatience verging on panic and so on… One has to wonder how this has an impact on our motor skills. Cutting edge Neurosurgery, or complex sports at the highest level, is a function of skills and attitude. These skills can be attained by constant practice. However, attitude takes a long time of conditioning to change. For some, it never changes and this prevents them from joining the group of elites making them hesitant to taking up challenges. In this aspect, Neurosurgery can be compared to a Formula one racing or even a wing-suit jumper. If one looks at what can go wrong, these sports cannot

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even exist.... Yet, the beauty of an overtaking in F1 or witnessing the wing-suit jumper zooming past is a joy to behold. So, what exactly separates the ordinary from the elite in such cutting edge "walk on the high wire" jobs? It is fear, a very primal emotion associated with the amygdala, the Papez circuit and the hypothalamus. What is fear? The state evoked by threat. What is threat? That which causes fear!

The primitive nature of human emotion belongs to the mind that we share with animals as studied by Dr. Mac Curdy [2]. Hence, apart from the liability we as humans hold to fear, the fear of even being afraid is inevitable and the power to conquer this fear produces the feeling of excitement. Often fear of what can go wrong is what drives this anxiety, insecurity and anger. This is true in general atrocities like religious riots or coups and politicians are expert hands to make use of these fear/insecurities of the general public to incite them against certain sets of religions or individuals or parties. This manipulation has been done from time immemorial and forms an interesting part of political studies. From the viewpoint of an aneurysm surgeon, the fear of failure or the fear of imminent rupture of an aneurysm has to be kept in a different drawer of the mind. Fierce focus will help the surgeon to do this and bravery is not about doing foolish things but is rational about each step and achieves a little bit more towards clipping the aneurysm.

Neurobiology of Fear

To understand the neurobiology of this feeling one must know about the Papez circuit which conveys the information from amygdala to the hypothalamus resulting in the sympathetic reactions like increase in heart rate, perspiration and the urge to run away. This is the same circuit which causes your knees to buckle and your chest to burst when you would propose to your lady or do something out of the ordinary! The same circuitry is at use when a boxer or a cricketer sledges the opponent trying to get him mad and behave in an irrational manner ultimately losing his "cool" and his wicket or the boxing match. The same happens during an aneurysm repair or a very difficult tumor surgery during which the "red haze" of fear or impatience leads to degeneration of motor skills of the neurosurgeon, unnecessary hurry or an urge to finish things off as fast as possible leading to disasters.

The sensory information from all the senses is conveyed to the amygdala and the entorhinal cortex, which is the primal centre for fear. The stria terminalis, a pathway leading from the amygdala to the hypothalamus, results in the manifestations of fears as all of us know. The three distinct sites responsible for provoking a fear response via electrical stimulation are the lateral and central zones of amygdala, the anterior and medial hypothalamus and some specifies regions of the PAG [3]. The most critical component comprising the central neural circuitry for fear learning is the amygdala [4]. Comprised of a heterogenous group of neurons, which are often subdivided into subnuclei each responsible to play separate but complementary roles in acquisition, expression and extinctinction of fear. These group of neurons share properties of the cortex and stratum. The Basolateral complex (BLA) made up of Lateral (LA), basolateral (BL) and basomedial (BM) nuclei, regulates conditioned fear. The intercalated cell masses comprise of the central nucleus (CeA), further divided into lateral (CeL) and Medial (CeM) sub nuclei [5]. The lateral/basolateral nucleus is the site of plasticity underlying the learned association between the Controlled and uncontrolled Stimulus. The medial nucleus plays a modulatory role in the process of predator odor-induced fear learning, these

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areas have been the subject of extensive research and multiple reviews. Recent research suggests that the CeA, while initially believed to be primarily a final common output pathway of the fear circuit to the behavioral and autonomic effectors regions of the brain, is also involved in the acquisition, expression, and consolidation of conditioned fear. The CeL receives input from many extra-amygdalar sources, including the mPFC, pPVT, auditory thalamus and cortex, and several brain stem areas with projections releasing neuromodulators onto CeA cells, such as glucocorticoids, estrogen, CRF, and oxytocin. This leads to the working hypothesis that fear-related information is gated by local inhibitory circuits in the CeL as it passes from the BLA to the CEm and the activities of these local circuits are tuned by the cortical and subcortical inputs onto the CeL using neuromodulators. However, it is not necessary that all sensory inputs trigger fear. This is because of the the specific pattern of environmental cues confronting the organism. The impulse transfer from LA to CeM is flexibily gated and the CeL and the ICMs fulfill receive glutamatergic inputs from BLA and send GABAergic projections to CeM resulting in a structured response [4,6].

Can we measure this?

Prior researches have indicated that visualizing the amygdala and the stria terminalis and then visualizing blocking off the inputs from the amygdala to the hypothalamus is difficult to a great extent in the author's experience as a surgeon as well as somebody who has played different competitive sports including martial arts! This may work for people who understand this circuit and would need the others to understand and then visualize the circuit as well as blocking it. Controlled response in humans is assessed via psycho physiological measures like skin conductance response (SCR), galvanic skin reflex, electromyography (EMG)and changes in heart rate. [7].

Functional magnetic resonance imaging (fMRI) is a powerful tool for investigating the emotional and cognitive brain responses. The use of a functional MRI enables the measurement of fear conditioning process during which one can see the difference in their way of functioning. It detects changes in the cerebral blood flow as a result of neuronal activation across the brain, while a cognitive task is performed.

The non-invasive nature of fMRI, proves to be an invaluable tool to delineate neural systems underlying sensory processing and higher cognitive functions. The technique is sensitive to changes in brain function due to neuropsychiatric disorders, pharmacological changes and genetic differences [8] hence representing a valuable research and clinical diagnostic tool. However, the limited correlations using only animal studies (eg: rodents) can reveal causal mechanisms providing the opportunity for translational preclinical studies into the influence of pharmacological, genetic and environmental manipulations on brain function, which would be rather difficult to conduct in human subjects [9-10].

For example, a study conducted on awake rodent models showed activation of the amygdala and related fear circuitry in response to a fear-conditioned stimulus and also concluded the linear correlation of magnitude of fear circuitry following early life stress [11-12]. Another study using fMRI on persistent and desistent subgroups of childhood-associated disruptive behavioral disorders (DBD) showed enhanced neural responses during fear conditioning [13].

Therefore, in order to understand the circuit- and cellular-level contributions of the CeA to fear learning, it is important to obtain sophisticated functional data

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superimposed onto the existing anatomical framework. Fortunately, an increasing number of genetically encoded fluorescent sensors [14-15] and actuators [16-17] for optical recording and control of neural populations respectively are becoming available. These approaches, in combination with intersectional genetic methods [18] the power to extract this critical information [5].

Conclusion

The above study clearly indicates that some form of sequencing or calculation whilst perceiving the fearful or for that matter, any emotional stimuli might blunt the emotion and may not produce extreme emotions. This would be an extremely interesting and useful piece of information for many who are in cutting edge professions and competitive sports. Where we have reviewed an extensive literature on the neuro physio biology of fear conditioning, it is equally important to know the mechanism behind fear extinction- an attempt to conquer our fears. Conditioning or repeated exposures to similar scenarios help to a great extent and this is why veterans of war and of large number of surgeries behave in a way that is patient and rational and is able to tackle the situation at hand.

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Original Article

Prevalence of co-morbid conditions in Heart failure: an experience at tertiary care hospital

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Abstract

Introduction

Patients with heart failure (HF) have various co-morbidities that complicate management and may adversely affect outcomes. HF guidelines provide little discussion on this topic and evidence is sparse.

Material and Methods

This is a descriptive cross-sectional study on 240 consecutive patients with HF admitted from September 2016 to July 2017 at B.P. Koirala Institute of Health Sciences (BPKIHS), Nepal. All patients admitted with diagnosis of HF with reduced or preserved ejection fraction (NYHA functional class III/IV) based on Framingham Criteria and echocardiography assessments were included. Pre-defined co-morbid conditions were assessed.

Results

Mean age of patients was 53.5 years and 53% were female. Most patients were in NYHA class III or IV (25% and 75% respectively) and 28.3% had ischemia as a cause of HF. Among co-morbidities, 85% of patients with HF had at least one co-morbidity. Anemia (68.3%), coronary artery disease (30.4%), hypertension (26.6%), diabetes (18.7%) and chronic kidney disease (7.5%) were the co-morbidities with the highest prevalence. Chronic obstructive pulmonary disease (3.7%), sleep apnea (2.5%), hypothyroidism (2.5%) and stroke (2.5%) were less common. Of all patients, only 15% had no co-morbidity, 40% had one co-morbidity, 22% had two co-morbidities, and 13 % had three or more co-morbidities.

Conclusion

Co-morbidities are common problems and anemia is the most common in our scenario which could be of multi-factorial etiology. Careful attention to the diagnosis and management of specific co-morbidities may help to improve outcomes in patients with HF.

Keywords:

Co-morbidities, Heart failure, Prevalence

Introduction

HF is a clinical syndrome which is characterized by the heart's inability to meet the body's circulatory demands. HF is associated with high morbidity and mortality and poor quality of life [1]. There is increasing evidence that co-morbidities frequently accompany HF and lead to increased morbidity and mortality and a further decrease in quality of life [2]. Hospitalization rates are increased in the presence of co-morbidities.

The term co-morbidity can be defined as a medical condition existing simultaneously, is caused by or is otherwise related to another condition in the same patient [3].

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High prevalence of co-morbidities in patients with HF suggests a common risk factor or a causal relationship. It is believed that HF itself could be a cause of multiple other co-morbid illnesses [4].

In general, the prevalence of co-morbidities is high across all western studies [5,6]. There is paucity of data on these areas from our part of the world. Thus, this study was carried out to have insight about patterns of co-morbidities that will help to early recognition and treatment of these conditions.

Material and Methods

This is a cross sectional observational hospital-based study. Total of 240 consecutive patients (age $\geq$16 years) with diagnosis of HF who were admitted from September 2016 to July 2017 at division of cardiology, internal medicine ward of BPKIHS, Nepal were included in the study. The aim was to identify the pre-defined co-morbid conditions and their prevalence in patients suffering from HF. All patients admitted with diagnosis of HF with reduced or preserved ejection fraction (NYHA functional class III/IV) based on Framingham Criteria and echocardiography assessment were included.

Clinical and demographic variables were noted at admission which included age, gender, underlying etiology of HF and associated co-morbidities. Particular emphasis was given to pre-specified cardiac and extra-cardiac co-morbid conditions that directly or indirectly impact the manifestations of HF and its prognosis. Ethical approval was obtained from institutional ethical review board (IERB) prior to beginning the study. Collected data were entered in Microsoft Excel 2007 and converted into SPSS 21 version. For descriptive statistics: percentage, mean, standard deviation, interquartile range was calculated. Graphical and tabular presentation was made as necessary.

Results

The mean age of 240 patients was 53.5 (range 16-90) years and 53% were female. Most patients were in NYHA class III or IV (25% and 75% respectively) and 28.3% had an ischemic cause of heart failure. Eighty-seven (36.2%) patients were current cigarette smokers and 6.6 % had a significant history of alcohol consumption. Table 1 shows baseline characteristics of the study population. Among the co-morbidities, 85% of patients with HF had at least one co-morbidity. Anemia (68.3%), coronary artery disease (30.4%), hypertension (26.6%), diabetes (18.7%) and chronic kidney disease (7.5%) were the co-morbidities with the highest prevalence (Table 2). Chronic obstructive pulmonary disease (COPD) [3.7%], sleep apnea (2.5%), hypothyroidism (2.5%) and stroke (2.5%) were less common. Of all patients, only 15% had no co-morbidity, 40% had one co-morbidity, 22% had two co-morbidities, and 13% had three or more co-morbidities.

Among electrocardiographic abnormalities, around a third of patients had tachycardia, 25% had left ventricular hypertrophy, 23.3% had atrial fibrillation and 11% demonstrated inter ventricular conduction delay. Echocardiography revealed LV systolic and diastolic dysfunction in 75% and 82% of patients respectively, mitral regurgitation in 52%, right ventricular dysfunction in 24% and moderate to severe pulmonary artery hypertension in 86% of patients (Table 4).

Table 1: Clinical characteristics of patients with heart failure (n = 240)

Age in year (mean and range)	53.5 (16-90)
Male Female	113 (47 %) 127 (53 %)
Heart rate in bpm (mean and range) Tachycardia (Heart rate >100 bpm)	94 (60-160) 72 (30.6%)
Blood pressure in	

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mmHg(Mean and Range) Systolic Diastolic	112.4 (60-210) 72 (40-100)
Presenting symptoms at admission Dyspnea (NYHA class) IVIII Fatiguability Palpitation	 180 (75%) 60 (25%) 98 (40.8%) 20 (8.3%)
Clinical signs Crackles Edema Raised JVP	 219.1 (91.3%) 187.4 (78.1%) 160.5 (66.9%)

Table 2. Co-morbidities of patients with heart failure

Anemia	164 (68.3%)
Coronary artery disease	73 (30.4%)
Hypertension	64 (26.6%)
Type 2 diabetes mellitus	45 (18.7%)
Chronic kidney disease	18 (7.5%)
Chronic obstructive pulmonary disease	9 (3.7%)
Sleep apnea	6 (2.5%)
Stroke	6 (2.5%)
Hypothyroidism	6(2.5%)
Hyperthyroidism	3(1.25%)
Bronchial asthma	3(1.25%)
Hyperuricemia	3(1.25%)
Pulmonary embolism	3 (1.25%)

Table 3. Acute organs dysfunction and electrolytes imbalance in patients with heart failure

Organs dysfunction Acute Kidney injury Hepatitis	 33 (13.7%) 18 (7.5%)
Electrolytes imbalance Hyponatremia Hyperkalemia Hypernatremia Hypokalemia	 60 (25%) 19 (7.9%) 17 (7.08%) 17 (7.08%)

Table 4. Electrographic and Echocardiographic co-morbidities in patients with heart failure

Electrocardiogrphic findings	**Echocardiographic findings**
Tachycardia (>100) 74 (30.8%)	LVEF: Reduced 180 (75%) Normal (≥ 55%) 60(25%)
LVH 60(25%)	Moderate to severe PAH 207 (86%)
AF 56(23.3%)	LVDD 197 (82%)
LBBB 16(6.6%)	MR 125(52%)
RBBB 10(4.1%)	RV dysfunction 58 (24.1%)

Abbreviations: AF: Atrial fibrillation, RBBB: right bundle branch block, LBBB: Left bundle branch block, LVH: Left ventricular hypertrophy, LVEF: Left ventricular ejection fraction, PASP: Pulmonary artery hypertension, RV: Right ventricle, MR: Mitral regurgitation, LVDD: Left ventricular diastolic dysfunction

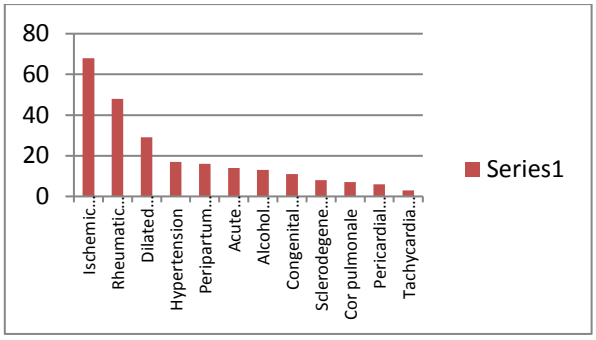

Figure 1. Etiologies of heart failure.

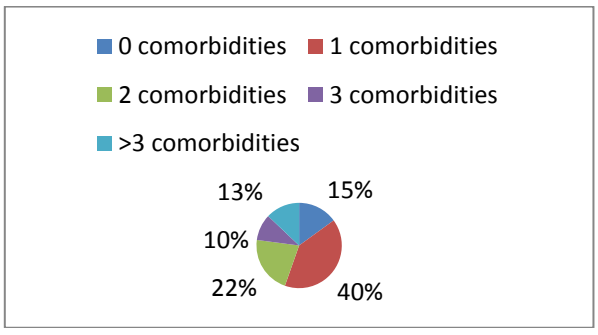

Figure 2. *Prevalence of co-morbidities in patients with heart failure.*

Discussion

This study focuses on co-morbidities of patients with HF of different etiologies. We found that the majority of patients had at least one co-morbid condition. Anaemia, coronary artery disease, hypertension and

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diabetes were the most common co-morbidities in our patients, along with COPD and chronic kidney disease which were less common. These findings are consistent with other studies [7, 8]. In developed countries, CAD leading to ischemic cardiomyopathy remains the commonest cause of HF as in our study. However, rheumatic heart disease leading to HF is more prevalent in this part of the world and we found 20% of patients hospitalized with HF had rheumatic heart disease. Table 5 shows the comparison of characteristics and prevalence of Co-morbidities in patients with HF among different studies from Nepal and western world.

Various studies show a high prevalence of co-morbidities in patients with HF. Although co-morbidities might cause HF, it is likely that HF itself could be a cause of multiple other co-morbidities [4]. Organs in HF may be affected by impaired haemodynamics, reflected by elevated systemic and pulmonary venous pressure, among other factors which plays a pathophysiologic role in renal and liver dysfunction [9]. In our study, acute kidney injury and congestive hepatitis were present in 13.7% and 7.5% patients respectively.

Anemia in patients with HF has been shown to be independently associated with increased risk of hospital admission and all-cause mortality. Prevalence of anemia in patients with HF and low ejection fraction range widely from 4% to 61% (median 18%) [10]. The most common co-morbid condition in our study was anemia (68.3%). The high prevalence of anemia in general population in Nepal may have contributed to the high prevalence [11].

Framingham Study [12] shows that hypertension is the commonest (75%) underlying disease contributing to congestive HF. In contrast, hypertension was reported to be the primary etiological factor in only 4% of HF patients in an overview of 31 studies [13]. In our study; however, only 26.65 % of HF patients had hypertension as a co-morbid condition indicating lower prevalence than western population.

Diabetes mellitus (DM) is associated with increased morbidity and mortality in patients with HF and it may complicate the clinical course of HF through different mechanisms, including electrolyte disturbances, increasing infection risk and altered drug absorption as well as through ischemia and other direct adverse effects on the myocardium [14]. We found 18.3 % of patients hospitalized with HF had Type 2 diabetes mellitus as comorbid condition.

Renal impairment is an established risk factor for adverse outcome in patients with HF [15]. Acute Decompensated Heart Failure National Registry (ADHERE) showed that more than half of acute HF patients had at least moderate renal insufficiency on admission which was associated with increased mortality [5]. We found that 13.7 % of patients hospitalized with HF had chronic kidney disease and 7.5% patients had acute kidney injury as comorbid condition.

COPD is found in approximately one-third of HF patients, with a slightly higher prevalence in HF with preserved ejection fraction (HFpEF) patients compared with HF with reduced ejection fraction (HFrEF) patients [16]. In our study, only 3.7% of patients with HF had COPD possibly due to under diagnosis and 26% of patients were current smoker. The specific rationale for the increased prevalence in HFpEF patients is unclear. COPD was suggested to cause proinflammatory state leading to endothelial and myocyte dysfunction with resultant myocardial fibrosis and clinical HFpEF [17].

The pathophysiology of HF along with HF therapies make patients prone for electrolyte disturbances, commonly found

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are hyponatremia, hypokalemia and hypomagnesemia [18]. An understanding of the development and nature of electrolyte disturbances gives insight about pathophysiology of HF. It also increases one's sensitivity to the presence of this condition and provides the management rationale. In our study, hyponatremia (25%) was relatively common as compared to other electrolytes disturbances.

Table 5. Comparison of characteristics and prevalence of co-morbidities in patientswith heart failure among different studies.

Characteristics	**ADHERE registry, 2001-2004 [5]**	**OPTIMIZE-HF registry, 2003-2004 [6]**	**Dubey L et al 2010-2012 [19]**	**Shrestha UK et al, 2015 [20]**	**Our study 2016-2017**
HF population	105,388	48,612	255	264	240
Mean age (years)	72.8+_14.1	73.2	57(11-95)	63.7	53.5
Male: Female ratio	49:51	48:52	62:38	40.5:59.5	47:53
Race	Caucasian ,African American	Caucasian ,African American	Nepalese	Nepalese	Nepalese
HFrEF	50	49	62	-	75
HFpEF	50	51	38	-	25
Risk Factors and co-morbidities					
Hypertension (%)	69-77	23	-	54.2	26.6
Type 2 Diabetes mellitus (%)	40-46	42	-	14.8	18.7
COPD (%)	27-33	28	-	17.1	3.7
Smoking (%)	-	17	31	67.4	36.2
Significant alcohol use (%)	-	-	-	14.4	6.6
Mean hemoglobin (gm/dl)	-	12.5	-	12.8	
Mean serum creatinine (mg/dl)	HFrEF: 1.6±1.3 HFpEF: 1.7±1.5	1.4 (1.1-1.9) 1.3 (1.0-1.8)	-	1.4	1.29
Atrial Fibrillation (%)	17-21	31	-	21.3	23.3
Etiology of Heart failure					
CAD (%)	50-61	46	36.5	29.5	30.4
RHD (%)	-	-	25.5	8.7 (VHD)	20
DCM (%)	-	-	14.5	21.6	12
CHD (%)	-	-	2.7	-	4.5
Cor pulmonale (%)	-	-	12.2	15.5	2.9

Limitations:

This was ahospital-based study in limited number of patients with inclusion of symptomatic patients only. Diagnosis of ischemic heart disease was based on history, risk factors, wall motion abnormality in echocardiography and may not be perfect because lack of coronary angiography in all cases. Similarly, distinction between AKI and CKD may not be correct owing to lack of previous renal function status and follow up data. Data on some of the co-morbid conditions like obesity, depression, musculoskeletal problems are missing.

Clinical Implications:

Although the presence of various co-morbid conditions associated with HF is common in clinical scenario, HF guidelines provide little discussion on this area and the evidence is lacking and mostly observational. Presence of one or more co-morbid conditions like anemia, hypertension, diabetes etc. increases the morbidity and mortality in patients with HF. There is a need for a critical reappraisal of

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management strategies in patients with HF in which clinicians target co-morbid conditions along with focusing the underlying cardiac dysfunction.

Conclusion

Majority of patients with HF have one or more co-morbid condition with an increased prevalence of anemia, hypertension, diabetes mellitus and renal dysfunction in the form of acute kidney injury or chronic kidney disease. Anemia is the most common co-morbid condition in our scenario which could be of multi-factorial etiology and needs especial mention. Careful attention to the diagnosis and management of specific co-morbidities in HF patients may help to improve patient outcomes.

Ethical Clearance

The study was approved by IERB of B.P. Koirala institute of health sciences prior to beginning of the study.

Competing interests

None declared

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Original Article

Profile on ECG Changes in different types of Stroke in Patients at Tertiary Level Hospital in Eastern Nepal

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Abstract

Background

Physician knew for centuries that primary cardiac disorders leads to stroke, but it is recent realization that strokes may produce cardiac abnormalities. It is essential to distinguish whether cardiopulmonary abnormalities are caused by the stroke or unrelated. It is very difficult to distinguish because pre-existing cardiac abnormalities are highly prevalent in stroke. This study is designed to see ECG changes in stroke that can help for further evaluation and management.

Methods and Materials

This descriptive Cross-Sectional hospital-based study was conducted to describe the ECG changes, character of ECG abnormalities in patients with stroke. All the patients admitted in the Nobel Medical College in one-year meeting inclusion criteria and residing in Eastern part of Nepal were included. Both Ischaemic and Haemorrhagic stroke were taken. ECG changes includes QTc-prolonged, AF (Atrial Fibrillation), T inversion, QRS prolonged, PR prolonged, ST elevation, ST depression, Hyperacute T wave in different types of stroke was evaluated on the basis of age, sex, smoker, HTN and DM.

Result

The total participants were 100. Out of which 65 were male and 35 were female and 72.0% were 60 years and above and 28.0% below 60 years with Mean Age in year ± Standard deviation of male and female was (64.74 ± 12.62) and (63.69 ± 13.53) respectively. Ischemic and Haemorrhagic stroke was 87.0% and 13.0% respectively. ECG changes were found in 84.0%.

Conclusion:

Ischaemic stroke (87.0%) was more common than Haemorrhagic stroke (13.0%). ECG changes were in 84.0% and QTc-prolonged (29.0%) was the most common followed by AF (27.0%).

Key words:

Atrial Fibrillation, CT-Head, Electrocardiography,Stroke.

Introduction

Heart electrical activity can be recorded over a period of time using electrodes placed on a patient's body. That is what we call as Electrocardiography. The tiny electrical changes on the skin that arise from the depolarizing heart muscle during each heartbeat are detected by those electrodes. CNS Infarction: - brain, spinal cord, or retinal cell death due to ischemia, based on: Pathological, imaging, or other objective evidence of cerebral, spinal cord,

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or retinal focal ischemic injury in a defined vascular distribution or clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting > 24 hours or until death, and other etiologies excluded. Intracerebral Haemorrhage: A focal collection of blood within the brain parenchyma or ventricular system, which is not due to trauma [1].

Physician have known for centuries that primary cardiac disorders can lead to stroke, but it is very much recent realization that strokes may produce cardiac abnormalities. Following stroke cardiac disturbances are common. So, it is essential to distinguish whether cardiopulmonary abnormalities are caused by the stroke or unrelated to it. It is very difficult to distinguish because pre-existing cardiac abnormalities are highly prevalent among stroke patients.

So this study is designed to see the incidence of ECG changes in different types of stroke. As we encountered different ECG changes in stroke, so this study may help and give some information regarding the ECG changes and to carry out with the further evaluation and diagnosis of the patient. Also, in the previous study ECG changes were evaluated in patients with cardiac diseases but this study has rule out the cardiac diseases from the study participants prior to Stroke. So, it has been challenging to find out the cases with ECG changes without the cardiac diseases as most of the patient with stroke come with the history of pre-existing cardiac diseases.

Previous study conducted reveals that regional left ventricular wall motion is common to SAH and possibly with other types of stroke in the absence of CAD. So if in those cases ECG changes may be mistaken for cardiac cause and patient got thrombolysed may lead to ultimate death of the patient would be the curse to medical science so this study aims to find the different ECG changes in patient with both Ischemic and Haemorrhagic Stroke.

Previously, as this type of study was not conducted in our part of the country so this study might be helpful to the other physician to know the incidence of ECG changes in patients with stroke and formulate the treatment accordingly. Also, it is mandatory to do CT-Head in patient with stroke and also the ECG. So, this study is cost effective as well as Non-Invasive to the patient.

Material and Methods:

The is a descriptive and cross-sectional study, which was conducted only after getting Ethical Committee approval from Institutional Review Committee (IRC), Nobel Medical College, Kathmandu University. Patients and their care-givers were explained fully about study design, benefit and risks involved in the procedure and a duly signed written consent was taken from each patient. It was a descriptive cross-sectional study over a period of one year from April 2014 to March 2015. All patients from various parts of Eastern Nepal attended at Nobel Teaching Hospital Medicine department with Stroke as proved by CT-Head and ECG changes without any structural cardiac diseases had participated in this study.

Inclusion criteria:

Both male and female with age between 25-89 years diagnosed as Stroke clinically and with documented CT-Scan who gave written/verbal consent (consent can be given by the closest relatives of the patient if patient clinically unstable).

Exclusion criteria:

All patients less than 25 years old and more than 89 years old brought dead or who expired at emergency room, patients with previous documented cardiac disease and patients unwilling to undergo the study were not enrolled.

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The ethical approval was taken from IRB.The patients arriving at emergency department with stroke symptoms was routinely examined and accordingly managed at emergency room (casualty).The patients were then admitted to Medical Ward/ ICU with respect to his/her clinical condition.ECG and CT scan of head was done at the Emergency/Medical ward/ICU and CT-Scan if necessary was repeated.For all patients who fulfilled the inclusion criteria was enrolled in the study.Other routine laboratory tests were done.Clinical diagnosis of the patients was made.Duration of stay at hospital and clinical condition of the patients was noted.Study questionnaire and consents was informed and recorded in predesigned proforma. The data thus obtained from the study was statistically analyzed in MS Excel 2007 and converted it into SPSS17 (Statistical Presentation Systemic Software).For the descriptive study: Percentage (%), Mean, Standard Deviation was calculated and also the graphical and tabular presentation was made. Categorical data was evaluated by Chi-square test (Pearson's Chi−Square). Level of significance for all analytical tests was set at 0.05 and p value ≤0.05 was considered significant.

Results

This study is a descriptive cross-sectional study conducted over one-year period. All patients from various parts of Eastern Nepal attended at Nobel Teaching Hospital Medicine department with Stroke and ECG changes without any structural cardiac diseases is participated in this study. There were total of 100 patients that were enrolled in the study. Out of which 65(65.0%) are male and 35(35.0%) are female.

Table 1: Mean age and standard deviation of male and female patients.

Sex of the patient	Mean ± Std. Deviation	N
Female	63.69 ± 13.53	35
Male	64.74 ± 12.62	65
Total (n)		100

Table 2: Comparison of ECG changes in Ischaemic and Haemorrhagic Stroke on the basis of Age.

Age in years	≥60		<60	
	Ischaemic	Haemorrhagic	Ischaemic	Haemorrhagic
Normal	7	2	6	1
QTc-prolonged	19	3	6	1
AF	17	3	6	1
T inversion	8	0	1	0
QRS prolonged	6	0	1	0
PR prolonged	1	1	2	0
ST elevation	1	1	1	0
ST depression	2	0	1	0
LVH	0	0	1	0
T Hyperacute	1	0	0	0
Total	**62**	**10**	**25**	**3**
P value	0.469		0.997	

On the basis of Sex, in male, QTc-prolonged is found in 17(28.81%) of the patient with Ischaemic stroke and 2(33.34%) patient with Haemorrhagic stroke. Similarly, AF is found in 17(28.81%) patients with Ischaemic stroke and 3(50%) patient with Haemorrhagic stroke. Similarly, QRS prolonged, T inversion, PR prolonged and LVH are found in 6(10.16%), 3(5.08%), 3(5.08%) and 1(1.60%) of the patient with Ischaemic stroke but above ECG changes are found in none of the patient with Haemorrhagic stroke. ST elevation is found in 2(3.30%) and 1(16.66%) of the male patients with

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Ischaemic and Haemorrhagic stroke respectively. (CI 95%, P value = 0.629)
In female, QTc-prolonged is found in 8(28.57%) of the patient with Ischaemic stroke and 2(28.57%) patient with Haemorrhagic stroke. Similarly, AF is found in 6(21.24%) patients with Ischaemic stroke and 1(14.28%) patient with Haemorrhagic stroke. Similarly, T inversion, ST depression, QRS prolonged and Hyperacute T wave are found in 6(21.42%), 3(10.71%), 1(3.57%) and 1(3.57%) of the patient with Ischaemic stroke. In patient with Haemorrhagic stroke 1(14.28%) patients have PR prolonged. ST elevation is found in none of the female patients with Ischaemic and Haemorrhagic stroke. (CI 95%, P value = 0.174)

Table 3: Comparison of ECG changes in Ischaemic and Haemorrhagic Stroke on the basis of Smoking.

Smoker	Yes		No	
	Ischaemic	Haemorrhagic	Ischaemic	Haemorrhagic
Normal	6	1	6	2
QTc-prolonged	13	0	12	4
AF	13	3	10	1
T inversion	7	0	2	0
QRS prolonged	4	0	3	0
PR prolonged	3	1	0	0
ST elevation	2	1	0	0
ST depression	3	0	1	0
LVH	1	0	0	0
T Hyperacute	1	0	0	0
Total	**53**	**6**	**34**	**7**
P value		0.613		0.731

Out of the 100 study participants, 31.0% and 69.0% are alcoholics and Non-alcoholics respectively. And out of the 31.0% alcoholics, 27(87.09%) and 4(12.90%) have Ischaemic Stroke and Haemorrhagic stroke respectively. Similarly, of the 69.0% Non-alcoholic 60(86.95%) and 9(13.04%) have Ischaemic and Haemorrhagic stroke respectively.
Out of the alcoholic's participants, QTc-prolonged is found in 8(29.62%) of the patient with Ischaemic stroke and none with Haemorrhagic stroke. Similarly, AF is found in 7(25.92%) patients with Ischaemic stroke and 3(75.0%) patient with Haemorrhagic stroke. Similarly, QRS prolonged, T inversion, ST elevation, PR prolonged and ST depression are found in 3(11.11%), 2(7.40%), 1(3.70%), 1(3.70%) and 1(3.70%) of the patient with Ischaemic stroke respectively. ST elevation is found in 1(25.0%) of the patients with Haemorrhagic stroke. (CI 95%, P value = 0.345)

Table 4: Comparison of ECG changes in Ischaemic and Haemorrhagic Stroke with and without HTN.

Hypertension	Yes		No	
	Ischaemic	Haemorrhagic	Ischaemic	Haemorrhagic
Normal	7	2	8	1
QTc-prolonged	13	2	12	2
AF	13	3	10	1
T inversion	6	0	3	0
QRS prolonged	5	0	0	0
PR prolonged	3	1	0	1
ST elevation	2	0	0	0
ST depression	3	0	0	0
LVH	1	0	0	0
T Hyperacute	0	0	1	0
Total	**53**	**8**	**34**	**5**
P value		0.842		0.249

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Table 5: Comparison of ECG changes in Ischaemic and Haemorrhagic Stroke in patients with and without DM.

Diabetes Mellitus	Yes		No	
	Ischaemic	Haemorrhagic	Ischaemic	Haemorrhagic
Normal	4	1	9	2
QTc-prolonged	6	1	19	3
AF	4	1	19	3
T inversion	1	0	8	0
QRS prolonged	4	0	3	0
PR prolonged	0	0	3	1
ST elevation	1	0	2	1
ST depression	1	0	1	0
LVH	0	0	1	0
T Hyperacute	0	0	1	0
Total	**21**	**3**	**66**	**10**
P value		0.842		0.249

Discussion

In this study, there were 100 patients, 65.0% were male and 35.0% were female patients. 72.0% were above or equal to 60 years and 28.0% were below 60 years. The mean age of male and female subjects was 64.74 and 63.69 years respectively. 31.0% and 59.0% were alcoholic and smoker respectively, 61.0% and 24.0% were Hypertensive and Diabetes respectively and 87.0% and 13.0% have Ischaemic and Haemorrhagic stroke respectively.

Out of the Study participants, Normal ECG changes, QTc-prolonged, AF, T inversion, QRS prolonged, PR prolonged, ST elevation, ST depression, Hyper acute T wave and LVH were found in 16.0%, 29.0%, 27.0%, 9.0%, 7.0%, 4.0%, 3.0%, 3.0% and 1.0% respectively. QTc-prolonged was found in maximum number of the patient i.e. 29% followed by AF which was found in 27% of the patients.

As per the study ECG changes were found in 84% of Patients with stroke. Similar study was conducted in 1979 by Goldstein DS as the electrocardiogram in stroke: relationship to pathophysiological type and comparison with prior tracings. In those Study ECG abnormalities was present in 92% of patients with acute stroke [1]. The most common abnormalities were also changes from prior tracings: QT prolongation (68, 45%), Ischemic changes (59, 35%), U waves (42, 28%), and arrhythmias (41, 27%).

In this study, QTc-prolonged was present in maximum number of patients (30.70% of patient with Haemorrhagic Stroke and 28.73% with Ischemic Stroke). This study was similar to the study conducted by Oppenheimer SM, Cechetto DF, Hachinski VC in 1990, Ibrahim GM, Macdonald RL in 2012, Khechinashvili G, Asplund K in 2002. According to the study, QT prolongation – The most common stroke-related ECG abnormality is QT prolongation, found in up to 71% of patients with Subarachnoid Haemorrhage, 64% of patients with Intraparenchymal Haemorrhage, and 38% of patients with Ischemic Stroke [2].

In this Study, AF was found in 27% of the patients. A study conducted in 1992 by Schuchert A, Behrens G, and Meinertz T reveal atrial fibrillation was the most common arrhythmia, occurring in 14% of patients. Advanced age, history of cardiovascular disease, and history of palpitations increase the likelihood of detecting post-stroke atrial fibrillation [3].

In this study, T inversion was found in 9 % of the study participants (found only in patient with Ischemic stroke). A study conducted in 1977 by Dimant J, Grob D concluded that T inversionis four times more prevalent in stroke patients. The characteristic large T waves previously known as "cerebral T waves" have been noted in 50 % of patients with Intracranial Haemorrhage and appear particularly common following left frontal haemorrhage [4].

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Another study conducted in 2013 by Sunil K Agarwal, Elsayed Z Soliman reveal, the most common ECG abnormalities associated with stroke were T-wave abnormalities, prolonged QTc interval and arrhythmias, which were respectively found in 39.9%, 32.4% and 27.1% of the stroke patients and 28.9%, 30.7%, and 16.2% of the patients with no primary cardiac disease [5].

In this study ST changes was found in 11% of the patient's. Out of which 63.63% have ST elevation and 36.36% have ST Depression (with ST depression present only in patients with Ischemic Stroke and ST-Elevation present in 7.6% of patient with Haemorrhagic and 2.2% of patient with Ischemic Stroke). Similar study was conducted in 1974 by Lavy S, Yaar I, Melamed E, and Stern S in 1993 by Vingerhoets F, Bogousslavsky J, Regli F, et al. ST segment alterations- Nonspecific ST Change occur in 22 % of patients with stroke. Patients with stroke have a 7 to 10- fold higher incidence of ST segment depression when compared with controls, particularly if the left middle cerebral artery territory has been affected [6-8], but this study was not conducted for the side of the Ischemia and Haemorrhagic Stroke. The study reveals ST changes appeared to be more common among patients with Ischemic Stroke than among patients with Haemorrhagic Stroke.

Conclusion:

ECG changes in different types of stroke is very much high. Ischaemic stroke (87.0%) was more common than Haemorrhagic stroke (13.0%) and QTc-prolonged (29.0%) was the most common ECG changes followed by AF (27.0%).

QTc-prolonged, AF, PR prolonged and ST elevation were found more in patients with Haemorrhagic Stroke than Ischemic Stroke. T inversion, QRS prolonged, ST depression, Hyperacute T wave and LVH were found in none of the patient with Haemorrhagic stroke.

On the basis of age, sex, smoker, alcoholic, HTN and DM, Ischaemic stroke was more common than Haemorrhagic Stroke and QTc-prolonged was the most common ECG changes followed by AF.

Abnormal ECG changes are common in patients with stroke. ECG and CT-Head should be done before initiating the treatment as ECG changes are not only due to Cardiac Diseases but also due to CVA.

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Original Article

Mortality pattern in Emergency Department of a Tertiary Care Center in Western Nepal

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Abstract

Background

There is abundance of evidence regarding various aspects of mortality in emergency department from different parts of world but there is limited number of studies on mortality in context of western Nepal. The objectives of this analysis were to review the demographical pattern of mortalities and define the cause and frequency of death in the Emergency Department (ED) of our institute within 24 hours of treatment process.

Material and Methods

A retrospective study was carried out evaluating all patients who died during the treatment process in the Emergency Department of Lumbini Medical College in a three and half year of period from January 2014 to June 2017.

Results

A total of 33,472 patients attended to ED with mortality rate of 36.4%, 33.6% and 28.2% on consecutive three years in which 110 deaths occurred. There were 66 (60%) male and 44 (40%) female. The highest mortality was seen after age of 60 years (range 2 month to 90 year). Non-communicable causes & stroke deaths were found to be higher in number. Most of our patient n=52 (47.3%) death occurred within 6-12 hours of admission in ED.

Conclusion

Mortality within 24 hours of presentation at ED remains high. Well organized emergency setup, transport, development of protocol as well as new guideline will definitely help in reducing hospital mortalities.

Key Words:

Emergency, Mortality, Pattern

Introduction

Emergency Department (ED) is the first point of call for all critically ill in any hospital all over the world. In the ED, severity of various illness and injuries are seen and managed. Due to unplanned nature of patient attendance in emergency, the management of these patients is often challenging, so manpower requires immediate attention. The mortality and morbidity in the ED is directly related to the pre-hospital factors, adequate trained manpower and infrastructures [1-3].

There are many factors for deaths occurring in ED. These include poor pre-hospital care for ill and injured patients, distance between the patients place of abode and the hospital and the types of illness or injury. Also, the paucity of skilled manpower in many clinical fields and poorly equipped ED affect the mortality pattern [3,4]. It has been reported that 15-

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16 % of all the mortalities in a hospital occur in ED [5]. World Health Organization (WHO) claims that statistics on mortality pattern in ED should be available for evaluation of existing health care services which is a kind of managerial process in any health institute [6].

There are very limited numbers of studies on mortality pattern in context of Western Nepal. This study aims to seek the demographic mortality pattern and its causes in the ED of a tertiary center of Palpa within 24 hours of arrival.

Material and Methods

A retrospective review of the death records during admission at the ED of Lumbini Medical College Teaching Hospital was carried out over three and half year period from January 2014 to June 2017. Information was retrieved from patient case files and death certificates. Variables included were patient demographic data, clinical diagnosis, and duration of admission and time duration before death. All brought dead patients were excluded. The variables were analyzed in number and percentage by using SPSS 20.

Results

In a three and half year's period from January 2014 to June 2017, a total of 33,472 patients attended the ED. One hundred ten patients died giving a crude mortality rate of 0.33%. There were 66 (60%) male deaths and 44 (40%) female deaths, giving a mortality male: female ratio of 3:2. (Table 2)

Table 1: Mortality in various age group

Age Group	(n)	(%)
<10	3	2.7
10-20	2	1.8
20-30	1	0.9
30-40	10	9.1
40-50	15	13.6
50-60	17	15.5
60-70	31	28.2
>70	31	28.2
Total	**110**	**100**

Table 2: Mortality in both sexes in each year

Year	Sex		Total n(%)
	Male n(%)	Female n(%)	
2014	23 (20.9%)	17 (15.5%)	40 (36.4%)
2015	25 (22.7%)	12 (10.9%)	37 (33.6%)
2016	16 (14.5%)	15 (13.6%)	31 (28.2%)
2017	2 (1.8%)	0 (0%)	2 (1.8%)
Total	66 (60%)	44 (40%)	110 (100%)

The month with the highest proportional mortality was in August. The mortality rates were 36.4%, 33.6 %;28.2 % and 1.8% in consecutive three and half years (Table No: 2). The highest number of deaths recorded was in above 60 years of age (Table No 1). The non-communicable cause for death 101 (91.8%) was found more than communicable causes 9 (8.2%). Stroke was found to be leading cause of death n = 16 (14.5%) followed by acute myocardial infarction n = 15 (13.6%), upper GI bleeding n = 14 (12. 7%) and pneumonia n = 14 (12.7 %) (Table No 3).

Table 3:Clinical causes of patient death in Emergency Department

Causes of Death	Number	Percentage
Upper G.I. Bleeding*(Esophageal varices, Gastric and esophageal cancer, Peptic ulcer diseases)*	14	12.7
Tetanus	1	0.9
Stroke	16	14.5
Sepsis	6	5.5
Poly trauma	2	1.8
Poisoning	1	0.9
Pneumonia	14	12.7
Intestinal perforation	3	2.7
Intestinal obstruction	1	0.9
Hepatic Encephalopathy	2	1.8
Heart failure	2	1.8
Head injury	8	7.3
Hanging	1	0.9
Chronic kidney disease	5	4.5
Chronic obstructive pulmonary disease	4	3.6
Alcoholic liver disease	5	4.5
Acute respiratory failure	7	6.4
Acute respiratory distress syndrome	2	1.8

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Acute Myocardial infarction	15	13.6
Acute leukemia	1	0.9
Total	110	100

Stroke was the main cause of death in above 70-year age patients and comorbid conditions associated with stroke death were hypertension, diabetes mellitus and valvular heart disease. Eight (7.3%) mortalities were recorded from head injury, seven (6.4%) acute respiratory failure and six (5.5 %) sepsis. Fifty-two (47.3%) died within 6-12 hours of arrival (Table No 4).

Table 4: Time Duration before death

TimeIn hours	Number	Percentage
<1	6	5.5
1-6	48	43.6
6-12	52	47.3
12-24	4	3.6
Total	110	100

Discussion

Any hospital in the community can provide scientific information on the pattern of hospital death which is a useful indicator of its health situation. The study had a high female to male ratio of Emergency attendance but many studies in Africa have shown the male attendance in ED were more than female [7]. Among 33,472 patients attended in ED, 110 deaths were recorded with a mortality rate of 0.33% but the mortality rate reported by several studies done in hospitals of Nigeria were in the range of 2 - 6.8 % [3-8]. We observed a gradual decreasing in mortality rates in three consecutive years that may be due to increased health awareness in people as well as easy health facilities in sub urban & urban center.

In our research, highest mortality rate in male compared with female patients followed the pattern reported by other studies [9,10]. Male death was found to be higher and may be related to more prevalence of non-communicable infectious disease like chronic hypertension, Ischaemic heart disease, chronic alcoholism, neoplasms etc and probably male are more involved in high risk activities to earn their living [11]

The most deaths were recorded after the age of 60 years. Beckett et al reported 66% of death in three London EDs in patients over 60 years but in many studies had shown that most deaths were seen in young patients [3,12,25].

In our study, 91.8% of deaths were from non-communicable causes which were comparable to the report from new WHO Report [13]. It may be due to the improved personal hygiene and good immunity power after repeated coverage of national immunization program within the country.

The cause of death may vary from country to county. In our study, stroke was the commonest cause of death (14.5%) and head injury being relatively less (7.3%). The relative high stroke deaths may be due to uncontrolled or poor hypertension states; also, hypertension is a recognized independent risk factor for death. Many papers revealed that stroke and motor vehicle accidents (MVA) were found to be leading causes of deaths unlike several reports of urban and semi-urban tertiary health centers, road traffic accident (RTA) was leading cause of death [3,10,14]. The stroke mortality may reflect the quality of medical care available at emergency or uncontrolled hypertension to cause stroke [15,16]. Cardiac causes were predominant in Europe, USA and some Non-Western nations [12,17,18].

In our study acute myocardial infarction being the second most common cause (13.6%) followed by Upper GI Bleeding (7.3%) acute respiratory failure (6.4%) and sepsis (5.5%). Myocardial infarction / Ischemic heart disease was the commonest cause of death (55.56%) as shown in the study of Beckett et al [12]. In the study of Khan et al, sepsis (23%) myocardial infarction (19.7%) stroke (10.7%) and

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pneumonia 8.2%) were the leading causes of death [19].

Our study showed 47.3% of death was in between 6-12 hour of arrival followed by 43.6% in 1-6 hours & and 5.5% in less than 1 hour of arrival. Ekere et al found that 70.9 % cases died within 6 hours of arrived in ED and Rukewe et al reported it to be 43.4% within 5 hours of arrival [3,20]. In the limitations of our study, firstly it is a single hospital-based study where patients might be inadequate for critical analysis to meet the objective of the study. Secondly, most of the patients who died in ED had no post mortem examination for actual cause of death.

Conclusion

Stroke was found to be the major non-communicable disease related death presenting in ED. Most of the deaths were recorded after 60 years of age, which occurred within 6-12 hours of admission. Such high mortality in ED may be multi-factorial such as lack of pre-hospital care, late in presentation, delayed referral system, high poverty level causing poor access to quality health care.

So, promotion of an adequate and competent manpower in ED, efficient pre-hospital care, well organized ambulance service, vital infrastructures such as diagnostic and therapeutic facilities would help in reducing the emergency mortality.

Conflict of interest: None

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Original Article

Farm related and Wild Animals inflicted injuries related to Orthopaedics: Epidemiology and prospects for control

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Abstract

Background

Farm related and wild animals inflicted injuries in Orthopaedics is one of the major concern in developing countries like ours. As we don't know much about such injuries, it would be landmark study for our country. Therefore, the study helps us know better about its epidemiological aspects.

Materials & Methods

This prospective case series of farm related and wild animals inflicted injuries related to Orthopaedics, conducted from May 2006 to April 2008 at Department of Orthopaedics of B P Koirala Institute of Health Sciences, consisting of 87 patients admitted to the Orthopaedic ward, is presented. The preformed structured proforma were used to record the data and, later those records were analyzed.

Results

78 domestic related injuries and 9 wild animal related injuries were recorded in the recruitment period of two year. 23 femoral fractures, 14 humeral fractures, 11 Cervical spine injuries, 10 leg bone fractures, 9 forearm fractures were found. Fall from buffalo, Hit by buffalo were common cause of injuries in domestic related injuries whereas Hit / kick by elephant, attack by bear were causes of wild animal related injuries.

Conclusion

This study concluded that all adolescents and adults, of all age group and sex, should be included in community education and intervention programmes for prevention of such injuries. The prevention of this type was necessary.

Key words:
Farm, Domestic, Wild, Animals, Public Health

Introduction

It has been studied that injury rates for farming and non-farming sources were 1,683 and 6,980 per 100,000 persons, respectively. Animals (40%) were the primary sources of the farming operation related injuries; sports/recreation sources (61%) were associated primarily with non-farming related injuries. 83% of farming and 90%, of non-farming related injury required some type of treatment for them injures; in detail, 17% and 24%, respectively, were constrained from regular day to day works for one month or more [1].

Cases of Orthopedic related injuries inflicted by farm related and wild animals were encountered in Emergency room and Outdoor Patients Room of a tertiary care center of Eastern Nepal. This study was focused on collecting data regarding the type of domestic and wild animals inflicted injuries. The socio-demography of the affected

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patients, the type of injuries and its severity were noted. The purpose of this effort was to identify the incidence and consequences of animal inflicted orthopaedic related injuries and their potential risk factors. This study helps to assess the gravity of the problem and this area calls for preventive action.

Materials and Methods

This study was conducted in the Department of Orthopaedics, B. P. Koirala Institute of Health Sciences, Nepal, a tertiary care hospital, from 1st May 2006 to 30th April 2008.

All the patients attending Emergency Room and Out Door Patient Room with farm related and wild animal inflicted orthopaedic related injuries were included in the study. Following points were noted:

1. Socio-demography of the patient: Age, Sex, Occupation, Address, Cause of Injury
2. Type of injury
3. Anatomical structures inflicted
4. Neurovascular structures severance
5. Surgical interventions done
6. Follow up of 3 wks, 6 wks and 3 months
7. Total expenses for the treatment (Direct cost)

Above mentioned data were collected in the pre formed proforma, and entered into EXCEL 8. The entered data is analyzed with the help of EPI INFO.

Results

The study consists of 26 females and 61 males with mean age of 44.269± 23.425 yrs and 38.06 ±20.88 yrs (P-value =0.2248). Mean duration of reporting time to hospital is 67.72 hrs with SD of 106.47. Commonly farmers, housewives and students were involved in such type of injuries and details as shown in Table 1.

Table 1 showing different occupations of study population

Occupation	Frequency	Percent
Farmer	36	41.4%
Housewife	21	24.1%
Laborer	7	8.0%
Serviceman	1	1.1%
Shopkeeper	2	2.3%
Student	20	23.0%
Total	87	100.0%

In the study, 78 patients were found to be injured due to domestic animal related injuries where as 9 were due to wild animal related injuries. 7 patients were brought death in Emergency due to attack by wild elephants from various districts of Eastern Nepal. Mode of injuries by animals with frequency in details is shown in Table 2. Most of the patients reporting to our hospital were from Terai districts followed by hilly districts of Eastern Nepal as showed in Table 3.

Table 2 showing Mode of injury by domestic and wild animals

Mode	Frequency	Percent
Bear Bite	4	4.6%
Dragged by the rope of Bull	2	2.3%
Fall from Buffalo	17	19.5%
Fall from bullock cart hit by Bull	5	5.7%
Hit and thrown by Elephant	5	6.6%
Hit by buffalo	16	18.4%
Hit by Bull	12	12.3%
Hit by cow	11	12.6%
Hit by goat	2	2.3%
Hit by Horse	1	1.1%
Hit by Ox	12	12.5%
Total	87	100.0%

Table 3 showing no. of patients from different districts (region wise)

Districts	Region	Frequency	Percent
Siraha	Terai	19	22%
Sunsari	Terai	15	17%
Saptari	Terai	13	15%
Morang	Terai	11	12%
Jhapa	Terai	11	12%
Dhanusha	Terai	7	8%
Dhankuta	Hilly	3	3.5%
Udayapur	Hilly	3	3.5%
Bhojpur	Hilly	2	2.3%
Ilam	Hilly	1	1.25%
Terathum	Hilly	1	1.25%
Mahottari	Terai	1	1.25%

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Table 4 shows the different part of the limbs injured due to domestic and wild animal inflicted injuries. Among them, 23 femoral fractures, 14 humeral fractures, 11 Cervical spine injuries, 10 leg bone fractures, 9 forearm fractures were found. Unfortunately, all the cervical spine patients had traumatic quadriparesis. 23 patients had open fractures whereas 50 patients had closed fractures. Among open fractured patients, 5 had neurovascular deficit and 10 had tendon injuries.

Table 4 showing anatomical regions injured

Anatomical regions involved	Frequency	Percent
Arm and shoulder	19	21.83%
Forearm and hand	12	13.79%
Thigh and hip	29	33.33%
Knee / Leg and Foot	13	14.94%
Spine	14	16.09%

36 patients were treated conservatively whereas rest of the patients was treated with operative measures. Closed reduction and immobilization was done with Plaster of paris casts/slabs in the patients managed with conservative treatment. Different internal and external fixation devices (Plates and screws, Nails, External fixators, pins) were used to stabilize femoral fractures, Leg bone fractures, humeral fractures, forearm bone fractures. Direct cost incurred due to the injuries (Hospital stay + Drugs + Operative charges and Implants/ Plaster of paris) was NRs. 8524.4253 ± 4700.8836 with minimum of NRs 2000 to NRs 19500.

Discussion

It is alarming that traumatic injuries are increasing globally, moreover increasing trend in most developing countries, including Nepal. A large proportion of the injuries are caused by road traffic accidents, falls, burns, assaults, bites, stings and other animal-related injuries, poisonings, drownings/near-drownings and suicide. Globally, injuries are responsible for about five per cent of the total mortality, and the overall global annual costs were estimated huge amount of money. The burden and pattern of injuries in Africa and other developing areas are poorly known and not well studied. The increase in incidence is, partly due to rapid growth of vehicular transport, urbanization and expansion of industrial production without adequate safety precautions.[2] As we have also lacking such information in our country, this study will be initiation to know the status of such injuries in our country. A computerized search of the relevant literature regarding injuries related to agriculture was done and a manual search of journals publishing texts on health in low-income countries and in tropical environments was also done. A few studies on injury prevention policy and on research related to injury epidemiology and prevention have also been identified and included.

Although a few surveys and other investigations of injuries have been conducted over the years, injury epidemiology and control remain under-researched and relatively neglected subject areas. Much needs to be done. Collection and analysis of injury data need to be standardized, for example regarding age groups, gender disaggregation and severity. Injuries and accidents should be subdivided in at least road traffic injury, fall, burn, assault, poisoning, drowning, suicide, homicide and others, and details regarding time and place, victim and main cause should be noted. Morbidity survey field staff should be informed that injuries are part of the illness concept and that questions should be asked accordingly. Details regarding the circumstances surrounding different injuries must be known to those who develop preventive programs.

Injury is a public health problem affecting some people more than others. Our ordinary environment--the home, the work-site, the street or road--represents various kinds of risk, and some of these are difficult to

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eliminate. Occupational injuries can largely be prevented by well adapted environment and education in such places. Research is recommended in different areas. The outcome of emergency medical care and of different forms of transport and referral needs to be determined. This study helps us to know preventive interventions and its evaluation. Therefore it is intended to guide to highlight the need of a broader overview of the subject of such type of injury occurrence and prevention in Nepal, for example in preparation for the development of injury control programs or to help identify issues requiring further research in this field.

The study similar to our study was conducted to find out the incidence of and potential risk factors for farm-related injuries in Eastern Ontario. One hundred and seventeen dairy and beef farms were surveyed using a personal interview, comparing our study comprising total of 87 different injuries. Information was collected on demographic characteristics of the farm owners, workers, and families; characteristics of the farm operations; and information on behaviors potentially affecting injury risk, where as in our study we studied occupation, mode of injuries, geographical area and site of injuries. Ontario study showed that the overall farm injury rate was 7.0 persons injured per 100 person-years (95% C.I.: 4.9,9.1, n = 547). Common patterns of injury by ICD-9-E-Code included accidents caused by farm machinery (E919.0), accidental falls (E880-8), and injuries caused by animals (E906). Variables found in multivariate logistic models to be predictive of injury occurrence were living on a beef farm (RR = 2.5; p = 0.01); increased farm work experience (trend: p less than 0.01); full-time exposure to farm work (RR = 2.5; p = 0.04); and, in farm owners, the use of prescriptions medications (RR = 2.7; p = 0.07). Forty-six percent of the farm-related injuries were treated in a hospital-based emergency department (ER). Efforts to monitor the incidence of farm injuries using an ER-based information system have the potential to significantly under-estimate the scope of the regional farm injury problem in Eastern Ontario. [3] The study was significantly helpful to make our study more comprehensive as we needed prospective of this kind to find out RR and incidence in future studies on the basis of this study.

Studies from other developed countries have shown that agriculture is among the most dangerous occupational sectors in terms of work-related deaths. Pickett W et al. described the occurrence of fatal work-related farm injuries in Canada and compare these rates with those in other Canadian industries. The authors presented a descriptive, epidemiological analysis of data from the recently established Canadian Agricultural Injury Surveillance Program. Crude, age-standardized, age-specific and provincial rates of such injuries were presented, as are overall death rates in other Canadian industries. Other factors examined were the people involved, the mechanism of injury, and the place and time of injury. There were 503 deaths from work-related farm injuries during the study period, for an overall annual rate of 11.6 deaths per 100,000 farm population. High rates were observed among men of all ages and among elderly people [5]. In our study it was shown to be farmers and student involved in such injuries. Compared with other industries, agriculture appears to be the fourth most dangerous in Canada in terms of fatal injury, behind mining, logging and forestry, and construction. In our study it was found that farm related injuries were basically high in the rural part of eastern Nepal mostly in Terai belt than hilly area. It might be because of trandional farming in such area, poverty and lack of modern agricultural education.

Compare of others studies [2-5], injuries were of various grades, incapacitating patients to work in same job. This study also found out minimal to maximal direct

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expenditure due to such injuries and recommended to perform cost analysis in such injuries.

The study has its weakness due to low sample size and further detail analysis of injuries correlated to other aspects. However, the study was preliminary report of retrospective study of such injuries in our country, for those who are interested to know that such injuries can be of public interest and further research can be done in different aspects.

Conclusion

From the present study and different studies searched from literature shows that farm related and wild animals related injuries are one of the major factors of injury burden to most of the agriculture based developing countries. Therefore, these types of injuries warrant immediate action for control by different preventive measures mainly primary prevention by educating adolescents and adults groups associated with farming occupations.

Animal related injuries are a major but neglected emerging public health problem and contribute significantly to high morbidity and mortality worldwide. No prospective studies have been done on animal related injuries in our setting. This study was conducted to determine the management patterns and outcome of animal related injuries and their social impact on public health policy in the region.

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Original Article

Stillbirths - Determining the associated factors and causes according to relevant condition at death: an experience from Pokhara, Nepal

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Abstract

Background

Stillbirth contributes significantly to perinatal mortality. This study was conducted with aim to determine various factors associated with it and to define the causes of stillbirth according to relevant condition at birth.

Materials and Methods

This is prospective cross-sectional study conducted in the Department of Obstetrics and Gynaecology of Manipal Teaching Hospital from July 2015 to June 2017. All cases of stillbirth occurring during antenatal or intrapartum period after 28 weeks of gestation or fetus weighing 1000 grams or more were included. Detailed demographic parameters were noted. After delivery, fetus, placenta, umbilical cord and amniotic fluid were noted in detail. Data was entered in SPSS version 16 and analysis done.

Results

The stillbirth rate was 22 per 1000 births. Low educational level of women, lack of antenatal care, multiparous status, gestational age less than 34 weeks, low birth weight and male gender of fetus were found to be significantly associated with stillbirths. The cause of fetal death could be identified according to relevant condition at death in 84% of cases. Only in 16%, the cause of stillbirth was not identified. Intrauterine growth restriction was the commonest cause of stillbirth (22%), followed by congenital anomalies (15%) and hypertensive disorders of pregnancy (14%). Other causes were abruptio (7%), intrapartum asphyxia (7%) and rupture uterus (5%). Other minor causes were anemia, diabetes, cord prolapse and amniotic fluid abnormalities.

Conclusion

Low level of education, lack of quality antenatal care, multiparity, low gestational age and birth weight and male sex of fetus were factors associated with stillbirth. The cause of stillbirth was identified in most of the cases and largely was due to intrauterine growth restriction.

Key words:
Risk factors, ReCoDe classification, Stillbirth

Introduction

World Health Organization defines stillbirths as a baby born at 28 weeks of gestation or more with birth weight of 1000 grams or more or the body length of 35 cm or more. [1] Globally, at least 2.6 million stillbirths occur every year and most of them are attributable to preventable causes. [2,3,4] However, stillbirth was not recognized as a global burden of disease and were not tracked under the Millennium Development Goals and remained

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unconsidered as an individual death by International Classification of Disease till recent past. [1,2] Only recently has the 10th revision of the International Classification of Disease incorporated the deaths during the perinatal period and provided a system for classifying perinatal cause of death. [5] Moreover, stillbirth is not counted in the country data in more than 90 countries of the world including Nepal. [1,2]

Stillbirths contribute largely in the perinatal mortality of a country. However, the progress in reducing stillbirths is slower than that of the neonatal deaths. [6] This makes stillbirths one of the major public health burdens that has been overlooked. Stillbirth is a tragedy not only to the family but also to the treating obstetrician. Not only that a potential life was lost, mothers experiencing stillbirths suffer psycho-social consequences like anxiety, depression, stress disorders and stigmatization [1] and also the future prospects of fertility and pregnancy outcome becomes one the major concerns for them.

It has been observed that most of the stillbirths are preventable. [2,3,4] In order to prevent deaths, it is crucial to understand the factors associated with deaths and to know the causes behind the deaths. A clear understanding of cause of death is clinically vital in counseling the bereaved family about the loss and future prospects of pregnancy; in formulating and planning protocols for future gestation. At a policy level, identifying causes is important for managing strategies for prevention and prioritizing medical services at areas needed. Only then can the stillbirth burden be reduced.

Very few studies have been conducted in Nepal to identify the causes and associated factors despite the fact that it is a direct indicator of the quality of antenatal and intrapartum care of the woman. Causes of stillbirth can be analyzed by many different classifications but Relevant Condition at Death (ReCoDe) is the only classification system specifically developed for classification of the stillbirths unlike the other classification system and is specifically useful in developing countries where extensive investigations to determine the cause may not be possible [7].

This study was conducted in order to determine the factors associated with stillbirth and to analyzing its causes according to Relevant Conditions at Death (ReCoDe).

Material and Methods

This was a prospective cross-sectional study conducted in the Department of Obstetrics and Gynaecology of Manipal Teaching Hospital from July 2015 to June 2017 for a period of 24 months. It is a tertiary care referral care centre of Western developmental region of Nepal.

The entire pregnant women admitted with intrauterine fetal deaths with gestational age more than 28 weeks were included in the study. Gestational age was calculated from the last menstrual period when the mother was sure of date. If she was not sure, then period of gestation was calculated from ultrasound dating of first trimester if available. Whenever the period of gestation could not be calculated, birth rate more than 1000 gm were taken as the cut off value for including the cases of stillbirth. The study also included mothers who were more than 28 weeks of gestation, who had a viable pregnancy at admission but fetal death occurred during hospital stay and the baby was delivered with no signs of life. Verbal informed consent was taken from the mothers after informing them about the nature of the study.

A detailed history pertaining to age, caste, area of residence, educational and antenatal booking status was taken and

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noted in the preformed proforma. History regarding the current pregnancy, obstetric history, past history of the mother was taken and noted. Gestational age, antenatal investigations, previous ultrasound were also noted. If they did not have any investigations, routine blood investigations like complete blood count, urine routine and microscopy, blood group, random blood sugar, serology for hepatitis B, C, HIV and syphilis were sent and reports noted. Serology for TORCH could not be sent as the test was not available at our centre. All the mothers with stillbirths were managed according to the hospital protocol.

For the mothers who had intrapartum deaths, labour events like the duration of labour, time of rupture of membrane, colour of liquor were also noted.

Once the delivery occurred, fetus, placenta and the umbilical cord were examined in detail. Fetus was weighed. Whether the fetus was fresh or macerated when born was noted. Fetus was also examined to see for any external anomalies. Placenta was weighed and examined for any morphological anomalies in placenta, point of cord insertion, presence of retroplacental clots, oedema and infarcts. The colour, odour and amount of amniotic fluid were noted at time of delivery. Umbilical cord was also examined in detail for the presence of true knots, length and the number of vessels. However, none of the deceased fetuses were sent for the postmortem examination.

For every case of intrauterine fetal death that occurred, two unmatched controls were taken. Controls were two patients delivering consecutively after delivery of stillborn. Controls were taken to analyze the association of the various risk factors for stillbirths. Information on age, caste, address, status of booking, educational level of mothers, parity, history of previous abortion or stillbirth, gestational age, birth weight and sex of fetus were taken from the controls. Data were entered in the proforma.

Each case of stillbirth was analyzed for the cause of death. All deaths were analyzed and classified according to Relevant Condition at Death (ReCoDe). This new classification system developed in 2005 helps in understanding the cause of stillbirths [7]. This classification system seeks to establish what had gone wrong than why it went wrong. According to this system, primary cause leading to death is first classified according to anatomical groups starting from conditions affecting fetus then to conditions affecting umbilical cord, placenta, amniotic fluid, uterus, mother, intrapartum, trauma and unclassified group. Each of anatomical group is further subdivided into pathophysiological conditions. Primary cause was identified as the first on the list that is applicable. When available, the secondary cause was also coded [7]. The classification system according to ReCoDe is given in table no 1.

Table 1: ReCoDe Classification System of Aetiological Classification of Stillbirths (relevant condition at birth)

Group A: Fetus	Congenital anomalies	**Group E: Uterus**	Rupture
	Infection		Uterine anomalies
	Non immune hydrops		Others
	Isoimmunization	**Group F: Mother**	Diabetes
	Fetomaternalhaemorrhage		Thyroid disorder
	Twin transfusion		Essential hypertension
	IUGR		Hypertensive disorders in pregnancy
Group B: Umbilical cord	Cord prolapse		Lupus or antiphospholipid syndrome
	Constricting loop or knot		Cholestasis

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	Velamentous insertion		Drug misuse
	Others		Others
Group C: Placenta	Abruptio	**Group G: Intrapartum**	Asphyxia
	Previa		Birth trauma
	Other placental insufficiency	**Group H: Trauma**	External
	Others		Iatrogenic
Group D: Amniotic Fluid	Chorioamnionitis	**Group I: Unclassified**	No relevant condition identified
	Polyhydramnios		No information available
	Oligohydramnios		

Data was analyzed using SPSS version 16. Simple percentage and Chi square test were used for statistical analysis and p-value <0.05 was considered to be statistically significant.

Results

There were total of 100 stillbirths during the study period. There were 4516 births during the study period giving stillbirth rate of 22 per 1000 births.

The demographic characteristics of mothers with stillbirths and controls are given in table no 2. On Chi square analysis, significant association was found with low level ofeducation (primary level or below) and poor antenatal supervision of mothers with stillborn babies compared with those of controls.

Table No 2: Demographic Characteristics of Mothers with Stillbirths and Controls

Characteristics	Cases of IUFD (n = 100)	Controls (n = 200)	p- value
Age (years)			
≤19	9 (9%)	19 (9.5%)	0.30
20-35	82 (82%)	172 (86%)	
≥35	9 (9%)	9 (4.5%)	
Caste			
Brahmin Chettris	48 (48%)	100 (50%)	0.06
Matawala	26 (26%)	70 (35%)	
Dalits	22 (22%)	28 (14%)	
Others	4 (4%)	2 (1%)	
Area of residence			
Rural	78 (78%)	151 (75.5%)	0.6
Urban	22 (22%)	49 (24.5%)	
Educational Status			
Illiterate	9 (9%)	4 (2%)	<0.001
Primary level	30 (30%)	36 (18%)	
Secondary level	33 (33%)	96 (48%)	
Higher Secondary level	22 (22%)	60 (30%)	
University level	6 (6%)	4 (2%)	
State of Booking			
Booked	10 (10%)	57 (28.5%)	<0.001
Booked at tertiary level care	27 (27%)	32 (16%)	
Booked at primary level care	54 (54%)	110 (55%)	
Unbooked	9 (9%)	1 (0.5%)	

Figures in the parentheses indicated percentage

The obstetric characteristics of the mothers with stillbirth in presented in table 3. On statistical analysis, multiparous status of mother, gestational age less than 34 weeks, birth weight less than 2500 grams and male gender was more common in stillborn fetus compared to the controls.

Table 3: Obstetric Characteristics of the Mothers with Stillbirths and Controls

Characteristics	Cases of IUFD (n = 100)	Controls (n = 200)	p-value
Obstetric History			
None	81 (81%)	153 (76.5%)	0.29
H/O Abortion	14 (14%)	41 (20.5%)	
H/O Stillbirth	5 (5%)	6 (3%)	
Parity			
1	41 (41%)	131 (65.5%)	< 0.001
2-3	54 (54%)	66 (33%)	

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≥4	5 (5%)	3 (1.5%)	
Gestational Age (weeks)			
28-34	51 (51%)	20 (10%)	< 0.001
35-37	14 (14%)	26 (13%)	
38-41	33 (33%)	147 (73.5%)	
≥42	2 (2%)	7 (3.5%)	
Birth Weight (gm)			
< 1000	6 (6%)	2 (1%)	< 0.001
1000-1500	32 (32%)	7 (3.5%)	
1500-2500	38 (38%)	55 (27.5%)	
2500-4000	23 (23%)	132 (66%)	
>4000	1 (1%)	4 (2%)	
Sex of Fetus			
Male	68 (68%)	102 (51%)	0.005
Female	32 (32%)	98 (49%)	

Figures in the parentheses indicated percentage

The classification of the causes of stillbirths according to ReCoDe is presented in table 4.

Table 4: Classification of Stillbirths by Relevant Condition at Death (ReCoDe)

Causes of Stillbirth		ReCoDe Primary Classification (n=100)	ReCoDe Secondary Classification System						
			IUGR	Abruptio	Oligo	Polyhydra	Hypertensive disorders	Anemia	Asphyxia
Gr. A: Fetus	Cong Anom	15 (15%)	4						
	IUGR	22 (22%)			3		5	1	4
Gr. B: Umbilical cord	Cord prolapse	1 (1%)							1
Gr. C: Placenta	Abruptio	7 (7%)							7
Gr. D: Amniotic Fluid	Polyhydram	1 (1%)							
	Oligohydram	4 (4%)							2
Gr. E: Uterus	Rupture	5 (5%)							5
Gr. F: Mother	DM	2 (2%)				1			
	Thyroid disorder	1 (1%)							
	HTN disorders	14 (14%)							
	Anemia	2 (2%)							1
	Fever	1 (1%)							
Gr. G: Intrapartum	Asphyxia	7 (7%)							
Gr. H: Trauma	External	2 (2%)		2					
Gr. I: Unclassified	Condition unidentified	16 (16%)							
Total		100 (100%)	4	2	3	1	5	1	20

Figures in the parentheses indicated percentage

ReCoDe classification could define causes in 84% of stillbirths. Only 16% of stillbirths were classified in Group I unclassified group as the condition that led to death could not be identified. Most of the intrauterine fetal death was due to intrauterine growth restriction (IUGR) (22%). This was followed by congenital anomalies (15%) and hypertensive disorders in pregnancy (14%). Secondary causes of death could be analyzed according to the ReCoDe classification 36 cases of stillbirth. They were intrapartum asphyxia, hypertensive disorder in pregnancy, IUGR. oligohydramnios, abruptio and anemia.

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Discussion

The definition of stillbirth varies from country to country across the world depending upon the availability of the technological advancements in the country to provide care in order to increase the chance of survival of the fetus born at a certain gestational age. The cutoff point of lower gestational age of 20 to 22 weeks are used by the upper and middle-income countries while higher gestational age of 28 weeks is used by low and lower middle-income countries [8]. In our study, a cutoff point of 28 weeks was used. Stillbirths occurring before 28 weeks are normal managed as missed abortion at our centre and since Nepal belongs to low income country, this definition was adopted.

The stillbirth rate in our study was 22 per 1000 births similar to that reported in most of low and middle-income countries. [8] In our study, women with stillbirths had low level of education, lacked antenatal care, were multiparous and had lesser gestation age. Stillbirths were also observed to be more frequent in fetus with birth weight below 2500gm and in male fetus. Another study conducted in Nepal also reported low level of education, multiparous status and lack of antenatal care to be associated with stillbirths. [9] Extremes of age at pregnancy, primiparity found to be associated with stillbirth in other studies was not found in our study [8]. Educating and empowering women is important as education among all is one of the major factors that affect health seeking behavior of the women and this in turn can bring about a favorable pregnancy outcome.

Stillbirths reflect the antenatal and intrapartum care of mothers. In our study, lack of antenatal care was significantly associated with the occurrence of stillbirths similar to other studies. [8,9,10,11,12,] Antenatal care not only provides opportunity for supervision of pregnancy but also allows educating the women about the danger signs that may necessitate immediate care. However, the quality of antenatal care also matters to a great extent in pregnancy outcome. It was observed in our study that 54 % stillbirths were in women who were booked at primary care level where antenatal care is provided by auxiliary nurse midwives (ANM) at primary health care centre or health posts. Lack of ultrasound and basic blood investigations that are so crucial in diagnosing various pregnancy complications at these centres hampers the quality of antenatal supervision provided. Improving the quality of antenatal care thus seems to be vital in bringing out best of results.

Gestational age at the time of delivery was a crucial factor for outcome of pregnancy as found in our study. More number of stillbirths was detected at lesser gestational age as in most of the other studies as well. [10,11,12,14-17] Similar association was found for the birth weight of fetus for known reasons.

In order to determine cause of stillbirths, it is imperative to follow a standard classification system. A number of classification systems of stillbirths are known but many of them report about two-third of the stillbirth as unexplained [7]. Classification systems that cannot define the cause of such high proportions of cases cannot be of help in improving the quality of care. When different classification systems had been evaluated, ReCoDe had performed fairly well and is also known as the only classification system known in classifying cause of stillbirths. [7, 8] It is also more suitable for developing country like ours where extensive investigations and postmortem of the fetus may not be possible. Hence, this classification system has been used in the study. In the present study, cause of stillbirths could be identified in 84% of cases as reported by Gardosi, J et al in

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2005. [7] Similarly, cause of stillbirths was identifiable in almost 90% of the cases in studies using ReCoDe classification system. [13, 14]

Intrauterine growth restriction was the major cause of stillbirths (22%) followed by congenital anomalies (15%) and hypertensive disorders of pregnancy (14%) in our study. Similar observation was made in studies using ReCoDe classification system. [7, 14] The fact that other studies [11,12,17] reported IUGR in comparatively fewer stillbirth could be due adoption of different classification in these studies. A hypertensive disorder in pregnancy was the major cause in some of the studies [11-13,16-17]. IUGR and hypertensive disorders were associated closely with stillbirths in a case control study done in Nepal. [9]

Fetal growth and the blood pressure of mother are two important factors assessed at the time of antenatal supervision. Improved antenatal care with early diagnosis and timely management of these two conditions would definitely assist in decreasing the stillbirth rate.

Congenital anomalies as the cause of stillbirth were found in 15% of our cases. Other studies also reported slightly lower figures [11-14,16]. Congenital anomalies diagnosed were neural tube defects (anencephaly, hydrocephalus), cardiac anomalies, duodenal atresia, gastrochiasis all of which could have been diagnosed early in gestation. All these anomalies were diagnosed on ultrasound and some also after delivery like anencephaly and gastrochiasis. As most of the women were not booked or booked only at health posts with no facility for detailed anomaly scan in pregnancy; late diagnosis of these lethal anomalies contributed in the stillbirths. A role of quality antenatal care can be emphasized here as well. Nayak SR et al reported congenital anomalies in 32% of antepartum fetal deaths as autopsy was conducted in their study [18]. It can be inferred that postmortem study of the stillborn can help in finding the cause in many cases where cause cannot be identified.

Intrapartum asphyxia accounted for 7% of cases of stillbirth similar to another study. [17] Ajini et al and Parihar et al reported intrapartum asphyxia in fewer cases. [13,14] Intrapartum care could be improved in order to lower occurrences of intrapartum accidents and therefore decrease fresh stillbirths due to intrapartum asphyxia.

The most common secondary code for stillbirth classification were asphyxia, hypertension, and oligohydramnios as in another study [13]. Asphyxia was the main secondary condition seen in our study also appears to be a preventable condition that can be achieved by proper antenatal and intrapartum care.

Most of the stillbirths in our study were preventable. Prevention of the stillbirth can be achieved by improved antenatal care and intrapartum management.

Conclusion

The stillbirth rate was 22 per 1000 births. Low level of education, lack of quality antenatal care, multiparity, low gestational age and birth weight and male sex of fetus were factors associated with stillbirth. The cause of stillbirth was identified in 84% of the cases; intrauterine growth restriction (22%) followed by congenital anomalies (15%) and hypertensive disorders (14%) were the main causes of stillbirths.

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Original Article

Cytological evaluation of breast lesion and its histopathological correlation in a tertiary care center

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Abstract

Background

Breast cancer is one of the commonest cancers in female. FNAC is safe and cost affective screening test for breast lump having both high sensitivity and specificity. Our aim is evaluation of diagnostic accuracy of fine needle aspiration cytology [FNAC] in diagnosis of breast lesions.

Material and Methods

All male and female patients with breast lesion were subjected to cytological evaluation of which many were followed up with histopathological evaluation to assess the diagnostic accuracy of FNAC.

Results

Out of 1088 cases diagnosed on FNAC, 703 cases (64.61%) were benign and 232 cases (21.3%) were found to be malignant. In our study the most common benign lesion was fibroadenoma and commonest malignant lesion was Duct carcinoma. Maximum cases of breast lesions in females were in the age group of 21- 30 years followed by age group of 31- 40 years. While maximum cases in males were in the age group of 31-40 years & 61-70 years. The sensitivity and specificity of FNAC for cyto-histo correlation were found to be 97.16% and 92.83% respectively.

Conclusion

FNAC is a highly sensitive and specific test for diagnosis and categorization of breast lesions into different categories of neoplastic and non-neoplastic breast lesions.

Keywords:
Breast Lump, FNA, Histopathology.

Introduction

World over FNAC has become widely accepted tool for diagnosis of breast lesions as it is safe and simple method with high diagnostic accuracy [1]. Its success is due to its accuracy and cost effectiveness and high accuracy for a breast lump. Therefore, it holds to have many advantages for patients and surgeons [2].

There are wide varieties of breast pathologies. It is postulated that the non-proliferative and inflammatory breast lesions do not increase the risk of cancer. There is mild to moderate risk with proliferative breast disease not showing atypia and with atypia respectively and higher risk of malignancy with carcinoma in situ [3]. The success rate of FNAC for obtaining a definite diagnosis depends on whether the lesion is palpable and also its size. FNAC has approximately success rates of 75–90% for palpable and 35-55%

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for non-palpable breast lesions respectively [4]. The use of core biopsy can be considered as an alternative but the procedure is more cumbersome, expensive and time consuming as compared to FNA procedure [5-6].

The present study supported FNAC as a first line of investigation in work-up of breast lesion. In the present study our aim is to categorize the types of various breast lesions on cytology, to determine the adequacy rate, diagnostic accuracy, sensitivity, specificity, and positive and negative predictive values of FNA in the evaluation of breast lumps. Cytology–histopathology correlation was also seen for better insight of breast lesions.

Material and Methods

Various techniques for obtaining specimen for cytology are: Fine Needle Aspiration (FNA) technique, Fine Needle Capillary (FNC) sampling, Smears from nipple discharge,

Scrape smears from ulcerated lesions and Cyst fluid of the patients. The study was carried for a period of two years, from 5th June 2015 to 20thJune 2017.

Equipment required for this purpose are Needles- 23-22 gauge, Syringes and syringe holder – Cameco Syringe Pistol with 10 cc plastic syringe, Sterile containers, Slides – clean, dry and free of grease, fixatives–Coplin jar containing 95% ethanol and Stains- May Grunwald Giemsa (MGG), and Papanicolaou stains. The study was carried after getting the approval from institutional review committee. The data was analyzed by SPSS 14.0.

Results

The present study is an observational study that includes all breast lesions, observational analysis of1088patients were subjected to cytological evaluation,1061 cases were female and 27cases were male. The microscopic description of the sample and the diagnostic categories used for the smear listed below, as per recommendation with further specific sub-categorization whenever possible.

Benign: when there is no evidence of malignancy with further description and classification. e.g. Finding consistence with Abscess or Mastitis, Fat Necrosis, Non-Proliferative Breast Disease, Proliferative Disease Without Atypia, Fibroadenoma, Pregnancy Induced or Treatment Induce Changes, etc.

Atypical / Indeterminate: When the cellular findings are not diagnostic, with further description e.g. Findings suggests Proliferative Breast Disease with Atypia (Atypical Hyperplasia Versus Low Grade Carcinoma), Fibroepithelial Lesions (Fibroadenoma Vs PT), etc.

Suspicious / Probably Malignant: When the cellular findings are strongly suggestive but not definitive of malignancy. Tissue biopsy is recommended for a definitive diagnosis.

Malignant: When the cellular findings are diagnostic of malignancy, with specific sub-typing of neoplasm whenever possible.

Unsatisfactory: When there is scant cellularity or air drying or distortion artifact. Dense hemorrhage or inflammation has obscured the smear.

Table 1: Categorization of breast lesions on cytology

Categories	No. of cases (%)
Benign	703 (64.61)
Atypical / Indeterminate	55 (5.05)
Suspicious/ Probably malignant	16 (1.47)
Malignant	232 (21.32)
Unsatisfactory	82 (7.53)
Total	1088

Maximum cases in females were in the age group of 21- 30 years (25.11 %) followed by 24.19 % in the age group of 31- 40 years. While maximum cases in male were in the age group of 31-40 years & 61-70 years (0.45 %) followed by in the age

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group of 41-50 (0.41%). Anatomical distribution of lesion was almost equal on left and right side. Majority of breast lumps were located in upper and outer quadrant of breast the left breast. Next common site was central region and least common site was lower inner quadrant. There were 88 cases with bilateral lump.

Table below shows the Nature of specimen along with sample procured under USG – guidance.

Table 2: Distribution of Patients based on different methods of cytology.

Nature of Specimen	No. of cases (%)	USG-guidance No. (%)	Total (%)
FNA / FNC from Lump/ Nodularity	952(87.48)	49(4.50)	1001 (91.99)
Only Nipple discharge	10(0.91)	0	10 (0.91)
Lump (FNA/ FNC) & Nipple discharge	2(0.13)	0	2 (0.13)
Scrape from ulcerated lesions	1(0.09)	0	1(0.09)
Cystic lesions	53(4.92)	21 (1.93)	74(6.85%)
Total	1018(93.56)	70(6.43)	1088

Table 3: Inflammatory breast lesions.

Inflammatory:	Total =87 cases, (7.9%)
Acute mastitis	48
Chronic mastitis	16
Non – specific granulomatous mastitis	11
Tuberculosis mastitis	2
Duct ectasia	1
Fat necrosis	5
Lactiferous duct fistula	3
Periductal mastitis	1

Sub-categorization of Benign Breast Lesion In inflammatory lesions -Acute mastitis top the list followed by Chronic mastitisand nonspecific granulomatous mastitis.

Table 4: Lactational and hormonal change.

Pregnancy and Lactational and hormonal changes	Total = 34
Galactocele	14 (1.28 %)
Gynaecomastia	19
Premature Thelarche	1

In hormonal mastopathy gynaecomastia was the commonest diagnosis with 19 cases and a single case of premature thelarche.

Table 5: Benign breast lesion.

Benign neoplastic breast disease	No. of cases = 542
Fibroadenoma	270
Benign proliferative breast lesion	60
Benign breast lesion	142
Benign Fibrocystic disease	5
Benign cystic lesion	46
Benign Phylloides tumor	8
Epithelial hyperplasia	7
Miscellaneous	4

Table 6: Atypical breast lesion with mild to moderate risk of cancer.

Atypical / intermediate	Total = 55 cases (5.05%)
PBD with atypia	34
Papillary lesion	8
Gynecomastia with atypia	1
Benign breast lesion with papillomatosis	1
Borderline phylloid tumor	1
Atypical ductal hyperplasia	7
Epithelial hyperplasia with papillomatosis	1
Fibrocystic disease with atypia	2

In benign neoplastic breast disease maximum no of cases was of Fibroadenoma (270cases) followed by Benign breast lesion. In miscellaneous group,1 cases were of epidermal cyst, 2 cases of lipoma and 1 case of microfilariasis. In Atypical/ Intermediate

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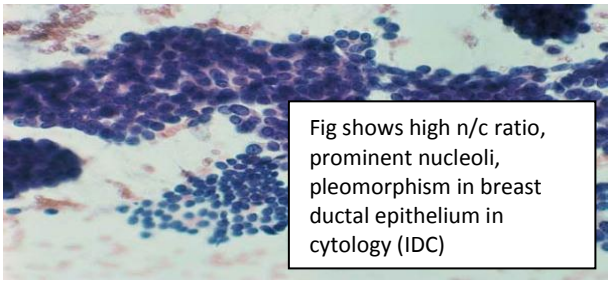
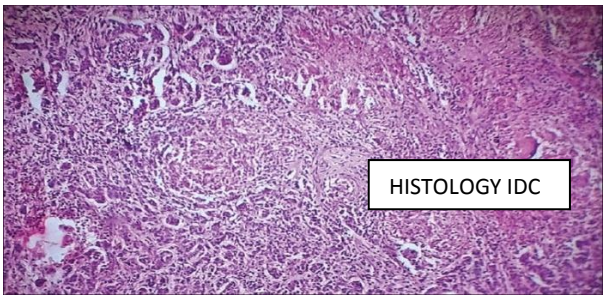
group Proliferative breast disease with atypia top the list with 34 cases followed by papillary lesion (8cases). In case of Suspicious / Probably malignant lesion, Atypical ductal hyperplasiatops the list followed by Low grade ductal malignancy.

Table 7: Malignant breast lesions.

Malignant lesion	Total = 232 cases
Ductal carcinoma (NOS)	163
Ductal malignancy with metastasis	51
Medullary carcinoma	1
Mucinous carcinoma	2
Lobular carcinoma	11
Invasive papillary carcinoma	1
Malignant phylloid tumor	1
Paget's disease	1
Primary lymphoid malignancy	1

In malignant lesion maximum no. of cases was from ductal carcinoma (214 cases, including ductal malignancy with lymph node metastasis) followed by lobular carcinoma (11 cases).





In present study follow up biopsies with cyto-histopathology correlation was available in 215 cases.

Table 8: Correlation of cyto& histological diagnosis.

Cytology		Histology	
Diagnosis	Number with follow-up biopsies	Benign	Malignant
Unsatisfactory	1	1	0
Inflammatory/Benign	152	151	1
Atypical/Indeterminate	18	15	3
Suspicious of Malignancy	11	4	7
Malignant	33	1	32
Total	215	172	43

In the present study, sensitivity was 97.16%, specificity was 92.83%, Positivity predictive value 91.15%, Negative predictive value was 97.74%, diagnostic accuracy was 94.70%, Adequacy rate was 92.36% and inadequacy rate was 7.63%.

Discussion

The objective of this study was to categorize and type the various breast lesions on cytology, statistically analyze the findings and correlate the cytology findings with histopathology for better insight of breast lesions on cytology.

The most common cancer in Nepal is cervix carcinoma followed by breast carcinoma. [7,8,9]. Different studies have shown that most commonly the lesions are benign for which only assurance is needed [8.9]. In order to prevent the cancer and for accurate approach to treatment, it is important to screen and diagnose the breast lesions early and categorization them into different groups of breast pathology [10,11]. Majority of breast lumps (55.05%) were located in the upper and outer quadrant of breast [12]. The commonest benign breast lesion is Fibroadenoma. Ferguson also reported that

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the commonest benign breast lump as fibroadenoma which most commonly occurs in the younger age group [13]. Singh A et al reported commonest malignant neoplasm of breast was Invasive duct carcinoma occurring most commonly in the age group of 41-60 years of age. In our present study we have similar findings.

FNA samples were categorized in to five categories (benign, Atypical, suspicious, malignant and insufficient). On cytological evaluation maximum cases were of benign breast lesions (64.61%) followed by malignant lesion (21.32%).7.53% cases were inadequate/insufficient for interpretation, while 5.05% cases were diagnosed as intermediate/Atypical breast lesions and 1.47% cases were categorized as suspicious /probably malignant breast lesions. Maximum breast lesions that occurred in the first 3 decades were benign, while malignant breast lesion was more common in the later decades (6^{th} decade onwards). Of the benign breast lesions, majority cases were of fibroadenoma (24.8%).

The Suspicious / probably malignant category included 16 cases in which the cellular findings were highly suggestive of, but not diagnostic of malignancy. In all these cases biopsy was advised. In malignant lesions, maximum cases were of Ductal carcinoma (NOS).

Histopathology correlation was available in 215 cases (19.76%). Maximum cases of histopathology correlation were found in the benign and malignant category, and lower cyto-histo correlation in suspicious lesions. The commonest cause of inadequate for interpretation on cytology could be attributed to marked sclerosis, hyalinized and collagenized stroma.

In the present study, sensitivity was 97.16%, specificity was 92.83%, positivity predictive value 91.15%, negative predictive value was 97.74%, diagnostic accuracy was 94.70%, adequacy rate was 92.36% and inadequacy rate was 7.63%. FNAC of breast lesions is highly sensitive, specific, and accurate screening test for palpable breast lesions in a tertiary hospital setting [14].

Conclusion

The FNAC of breast is cheap, safe and highly accurate investigation for diagnosis of breast lesions. The correlation between cytology and histology showed that FNAC is an accurate test in diagnosing and managing benign breast lesions.

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Case Report

A case report of Megalencephalic leukoencephalopathy with subcortical cysts, a rare inherited autosomal recessive leukodystrophy, in a Nepalese child

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Abstract
Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a rare inherited autosomal recessive leukodystrophy due to mutations in MLC1 or HEPACAM gene and have typical and characteristic neuroimaging findings. This article reports a case of 13 months old Nepalese male child with diagnosis of MLC.

Key words
Macrocephaly, Megalencephalic leukoencephalopathy with subcortical cysts, Nepalese

Introduction:
A rare inherited autosomal recessive leuko dystrophy, megalencephalic leuko encephalopathy with subcortical cysts (MLC) (Synonyms: Van der Knaap disease, Vacuolating Megalencephalic Leuko encephalopathy with Subcortical Cysts) was first reported by Singhal et al [1] and later described by Van der Knaap et al [2]. Of the clinical characteristics macrocephaly is the most consistent feature usually present at birth or developing during infancy with variable degree even up to 4 to 6 SD above mean. Other clinical manifestation of MLC includes mild motor developmental delay, seizures, pyramidal and cerebellar signs and mild delayed mental deterioration [3,4]. Wide age range from birth to 25 years for symptom onset with median age of 6 months is usually seen, however presentation even at fourth decade of life has been described in literature [4]. Mutations in MLC1 gene at chromosome 22q is found in about 75% of patients, whereas mutation in HEPACAM gene is responsible for remaining MLC patients [5]. Typical clinical presentation and characteristic neuroimaging findings helps establishing diagnosis of MLC. This article reports a case of 13 months old Nepalese male child with diagnosis of MLC.

Case presentation:
A 13 months old male child presented with complaint of one episode of seizure one week back and progressive enlargement of head noticed for 7 months of age. He was a second child born from non-consanguineous marriage with uneventful pregnancy and uncomplicated vaginal delivery. Social smile was attained by 2.5 months; head control by 6 months, sit without support by 8 months and stand without support by 11 months. However, since then regression of milestones was seen with inability to stand or sit without support. Similar history of progressive enlargement of head and regression of milestones was present in his older male sibling who died at the age of 3.5 years. No investigations were carried out in his older sibling. On examination macrocephaly

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was present with head circumference of 52.0 cm. Motor examination was normal. Computed tomography (CT) of brain was obtained which showed diffuse symmetrical white matter hypodensity in bilateral cerebral hemispheres with sparing of internal capsules and corpus callosum. Subcortical cysts of CSF density were present in bilateral anterior temporal lobes. Persistent cavum septum pellucidum was also noted. No change in appearance of lesions was seen in post contrast images. Basal ganglia, thalamus, brain stem and cerebellum were normal. (Figure: 1, 2, 3). Magnetic resonance imaging (MRI) of brain was suggested, but parents of child declined for further investigation. Considering clinical and CT scan findings diagnosis of MLC was made.

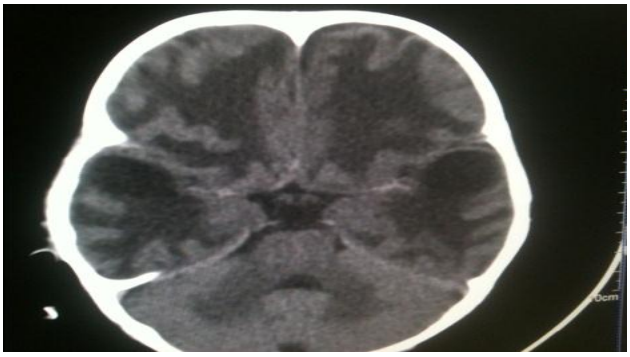

Figure 1

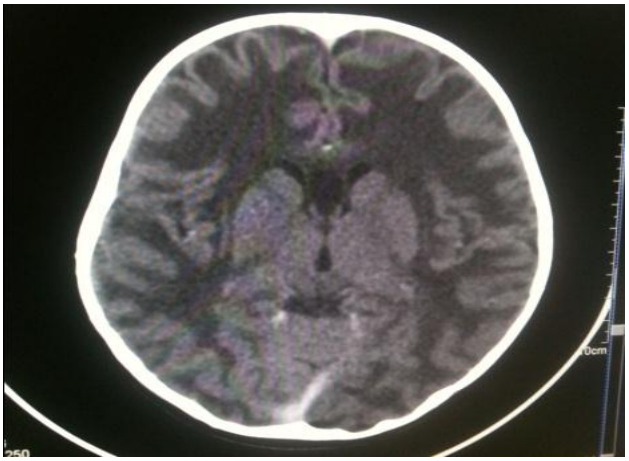

Figure 2

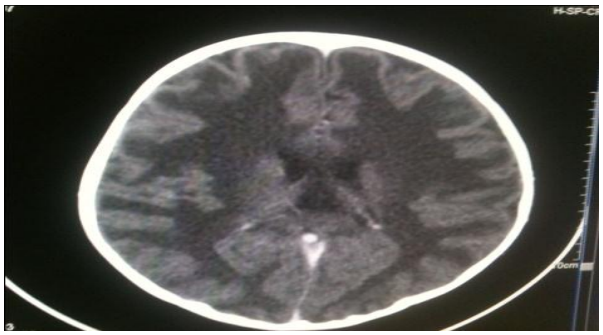

Figure 3

Figure 1, 2 & 3: Post contrast axial CT scan images of brain showing diffuse symmetrical white matter hypodensity in bilateral cerebral hemispheres with subcortical cysts in bilateral anterior temporal lobes. Persistent cavum septum pellucidum noted.

Discussion:

MLC is a rare inherited autosomal recessive leukodystrophy with mutations in MLC1 gene at chromosome 22q in about 75% cases and in HEPACAM gene in remaining cases [5]. It is more prevalent in certain ethnic groups like Aggrawal community in India, Libyan Jews and in Turks, and where consanguineous marriage is common [1,6-8]. In contrast a child in this case report was born from non-consanguineous marriage.

Typical clinical presentation and characteristic neuroimaging findings helps in establishing diagnosis of MLC. Macrocephaly is the characteristic and most consistent feature which is usually present at birth or develops during infancy with slow progression and delayed neurologic deterioration. Typical MRI findings are diagnostic for MLC. Diffuse symmetrical abnormal and swollen white matter of cerebral hemispheres showing confluent supratentorial white matter hyperintensity in T2 weighted and FLAIR images, and presence of subcortical cysts in bilateral anterior temporal lobes are typical. Cysts are also often found in frontoparietal region. These subcortical

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cysts are completely suppressed in FLAIR images and may increase in size and number later on. No changes in appearances of white matter abnormalities and subcortical cysts are seen in post contrast images. Basal ganglia and gray matter are not involved. Internal capsule, corpus callosum and brain stem are relatively spared, whereas white matter of cerebellum may show mild abnormality or may be normal [5,9]. Even though diagnosis of MLC can be made by clinical and MRI findings, chromosomal analysis for detection of mutations in MLC1 or HEPACAM gene should be performed to identify genetic mutations in the family and for prenatal diagnosis [6,9].

In differential diagnosis of MLC other conditions like Canavan's disease, Alexander disease, infantile onset GM2 and GM1 gangliosidosis, glutaric aciduria and merosin deficient congenital muscular dystrophy which also presents with macrocephaly and early onset leukoencephalopathy should be considered [3,8,10,11]. However, in comparison with these conditions, MLC shows slow progression of neurological deterioration. In contrast to MLC, in Canavan's disease there is involvement of basal ganglia and thalamus and subcortical cysts as seen in MLC are absent. Frontal dominance of white matter abnormality showing post contrast enhancement is noted in Alexander disease, whereas in MLC there is diffuse leukoencephalopathy and no post contrast enhancement. Also involvement of basal ganglia may be seen in Alexander disease. Involvement of basal ganglia and thalamus is seen in infantile onset gangliosidosis unlike that of MLC. In glutaric aciduria, apart from macrocephaly and white matter abnormality there is widening of CSF spaces along frontal and temporal convexity with widened bilateral sylvian fissures and bilateral basal ganglia abnormalities. Whereas in patients of merosin deficient congenital muscular dystrophy, subcortical cysts typically seen in MLC are lacking and patients have muscle weakness and hypotonia.

Conclusion:

MLC should be considered in differential diagnosis of a patient presenting with early onset macrocephaly with diffuse leukoencephalopathy. Even though MLC is more prevalent in certain ethnic groups and where consanguineous marriage is common, it can occur in child born from non-consanguineous marriage and found in Nepalese population. Typical neuroimaging findings are diagnostic for MLC which includes diffuse symmetrical abnormal and swollen supratentorial white matter with subcortical cysts in bilateral anterior temporal lobes. However further chromosomal analysis to be performed for detection of genetic mutation in the family and for prenatal diagnosis.

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