(JONMC)
JOURNAL OF NOBEL MEDICAL COLLEGE

VOLUME 1 2012 MAY-OCTOBER NUMBER 2

CONTENTS

Printed By: Panchakanya Printers, Biratnagar, Ph.021-525208, 525030 E-mail: panchakanyaprinters@gmail.com

(JONMC) JOURNAL OF NOBEL MEDICAL COLLEGE (Vol. 01 No. 02)

Journal of

NOBEL MEDICAL COLLEGE

(JoNMC)

(An official Medical Journal of Nobel Medical College)

Peer Reviewed Journal

VOL. 01 No. 02

Regd. No. 25161/060/61

MAY-OCTOBER, 2012

www.nobelmedicalcollege.com.np

SUBSCRIPTION CHARGES

	Annual	Per Copy
Nepal:	N.Rs. 200/-	N.Rs. 150/-
SAARC countries:	I.Rs. 150/-	I.Rs. 100/-
Other countries:	US$ 30/-	US$ 20/-

Subscription rated can be revised at any time without prior notice. Subscription request should be sent to the address given below. Subscriptions are to be sent in the form of bank drafts in favor of the "***Journal of Nobel Medical College***" payable at any bank either in Biratnagar or Kathmandu Nepal.

Address: Journal of Nobel Medical College (JoNMC),
Research and Publication Unit,
Nobel Medical College,
Kanchanbari, Biratnagar-5, Morang, Nepal.

Editorial correspondence:
Dr. Naba Raj Koirala
Chief-Editor
Journal of Nobel Medical College (JoNMC)
Nobel Medical College Teaching Hospital
Phone: 00977-21-460736 (Office)
Mobile: 9841318315 (Cell Phone)
Fax: 00977-1-460624
E-mail: drnabaraj@yahoo.com

Published by:
The **Journal of Nobel Medical College (JoNMC)** is published biannually by the Research and Publication Unit of Nobel Medical College, Biratnagar. The JoNMC publishes original articles in the field of Medicine and allied science s. Contributions are accepted for publication on the condition that their substance has not been published or submitted for publication elsewhere.

The JoNMC does not hold itself responsibility for statements made by contributors. Published articles become the property of the JoNMC and cannot be published elsewhere, in full or in part, without the written permission of the Editor.

Articles are invited for following sections: **Review article, Original Research Articles, Case Reports, Brief Communications & Letters to Editor**.

All the articles except Letters to Editors will be peer reviewed.

Published by:
Search and Publication Unit
NOBEL MEDICAL COLLEGE
KANCHANBARI, BIRATNAGAR-5, MORANG, NEPAL
Ph.No.: 00977-21-460735, 461736
Fax No.: 00977-21-460624

INSTRUCTIONS TO CONTRIBUTORS

The **Journal of Nobel Medical College (JoNMC)** is published biannually by the Research and Publication Unit of Nobel Medical College, Biratnagar. The JoNMC publishes original articles in the field of Medicine and allied sciences. Contributions are accepted for publication on the condition that their substance has not been published or submitted for publication elsewhere. The JoNMC does not hold itself responsib ility for statements made by contributors. Published articles become the property of the JoNMC and cannot be published elsewhere, in full or in part, without the written permission of the Editor. Articles are invited for following sections: **Review article, Original Research Articles , Case Reports , Brief Communications & Letters to Editor**. *All the articles except Letters to Editors will be peer reviewed.*

Two high -quality copies should be submitted and authors should keep one copy for reference. Articles should not be more than 5000 words long, must be typed on one side of t he paper only, double–spaced throughout (including references and tables) and with wide margins; all the pages, including the title page, must be numbered. Submission of the manuscript also on writable Compact disks is preferable.

Full Length Original Articles/Review article:

The **first page** should contain the full title of the article, name (s) of the author (s), in the order that is wished for publication, with their degrees, affiliations and complete addresses (specify the name and address for correspondence) and a running title not exceeding 5 words.
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.

Case Reports and Brief Communications:

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.

Letters to Editor:

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.

References:

These should be cited in the text by surname of first author and year of publication ***Vancouver system.*** On the page of References, they should be arranged in alphabetical order of first author. References should consist of names and initials of all authors, publication year, title of the paper, full name of the periodical, volume, and first and last page numbers.

(JoNMC)

Journal of Nobel Medical College

Editorial Office

Research and Publication Unit. **Nobel Medical College**, Kanchanbari, Biratnagar-5, Nepal
Phone: 021-461735, 460736. Fax: 021-460624
Email: drnabaraj@yahoo.com, dillikafle@yahoo.com

MICROALBUMINURIA IN HYPERTENSION: A REVIEW

Mahesh Bhattarai, Buna Bhandari

Abstract

Microalbuminuria appears early in the natural history of kidney disease. Hypertension accelerates the progressive increase in albuminuria and decline in glomerular filtration rate, albuminuria is the most important risk for progressive kidney injury. Greater urinary albumin excretion is due to increased glomerular hydrostatic pressure and increased permselectivity of the glomerular basement membrane. Reduction in albuminuria is protective for the development of complication, Angiotensin converting enzyme inhibitor leads to larger decrease in albuminuria when compared to other antihypertensive drugs.

Key word: Microalbuminuria, hypertension, Angiotensin converting enzyme inhibitor

Introduction

Patients with essential hypertension have a prevalence of proteinuria of 4% to 16%.[1]The prevalence of microalbuminuria varies enormously among different studies, with rates ranging between 5% and 37%.[2]In a study of 11,343 hypertensive patients without diabetes with a mean age of 57 years, microalbuminuria was present in 32% of the men and 28% of the women and increased with age and severity and duration of hypertension.

Pathogenesis of microalbuminuria in hypertension

Two mechanisms have been proposed for the greater urinary albumin excretion (UAE) in some patients with essential hypertension: increased glomerular hydrostatic pressure or increased permselectivity of the glomerular basement membrane.

Hemodynamic mechanism

Glomerular hydrostatic pressure is regulated by the relative vasoconstriction vasodilatation of the afferent and efferent glomerular arterioles. The tone of these arterioles is regulated by different mechanisms, and their sensitivity to pressor depressor substances also varies substantially. For example, the efferent arteriole is more sensitive to the pressor action of angiotensin II.[3] whereas the afferent arteriole is more sensitive to the vasodilator action of atrial natriuretic peptide. ACE inhibitors preferentially dilate the efferent arterioles.[4]

Normally, an elevation of systemic arterial pressure is associated with vasoconstriction of the glomerular afferent arterioles, which prevents transmission of the elevated hydrostatic pressure to the glomerulus and maintains the glomerular hydrostatic pressure unaltered.[5] This protects the glomeruli from the potential damages of hypertension. If the autoregulatory adaptation of the glomerular afferent arterioles is defective, increased glomerular hydrostatic pressure may ensue. Alternatively, an exaggerated vasoconstriction of the efferent arterioles may increase intraglomerular hydrostatic pressure; even in the presence of normal systemic pressure .derangements of these

adaptive mechanisms are important determinants for the susceptibility to develop progressive renal disease.

Renal function deteriorates faster in salt-sensitive than in salt-resistant hypertension. It was observed that greater UAE rates in salt-sensitive than salt-resistant patients, which was aggravated by a high salt intake. A significant correlation was present between intra glomerular pressure and UAE.

Several mechanisms could underlie sodium retention and the hemodynamic derangements in salt-sensitive patients with hypertension.[6] Those include increased activity of the sympathetic nervous system, the renin-angiotensin system, hyperinsulinemia, and decreased local production of vasodilator hormones. These renal hemodynamic abnormalities are probably genetically determined because they have been described in normotensive individuals with a family history of hypertension.[7]

The presence of microalbuminuria in patients with essential hypertension is also associated with decreased renal reserve. Ribstein et al described the presence of hyperfiltration in 12.5% of patients with hypertension. This increased to 27.5% when patients with body mass indices greater than 27 kg/m2 were included in the analysis. In this study, a significant correlation between UAE and filtration fraction was also described.[1]

Nonhemodynamic mechanism

UAE is not only dependent on renal hemodynamic factors, but also on the permselectivity of the glomerular basement membrane, and microalbuminuria could also be the consequence of loss of anionic charge of the glomerular basement membrane. Recent studies have shown an association between microalbuminuria and impaired glomerular charge selectivity even in healthy subjects. The increased permeability of the glomerular basement membrane for albumin could be caused by increased production by mesangial or endothelial cells of such factors as vascular endothelial growth factor and vascular permeability factor. Vascular permeability factor appears to be implicated in the pathogenesis of microalbuminuria and proteinuria in patients with diabetes148 and in those with glomerulonephritis.[1]

Microalbuminuria and serum lipid

In patients with essential hypertension , the combined presence of microalbuminuria and hyperlipidemia is frequent, and greater levels of UAE correlate significantly with greater serum levels of triglycerides and apolipoprotein B and lower serum levels of high-density lipoprotein (HDL) cholesterol. A possible cause for the association between microalbuminuria and hyperlipidemia could be an abnormal intake of lipids with the diet.However, microalbuminuria and hyperlipidemia are frequently linked independently of diet and/or body weight.[1]

Another explanation for the association between proteinuria and hyperlipidemia is that the urinary loss of protein may cause the increase in serum lipoprotein levels. An alternative explanation for the association between microalbuminuria and hyperlipidemia is that hyperlipidemia causes renal damage and the increase in UAE. Hyperlipidemia is a very well-known independent risk factor for atherosclerosis and cardiovascular disease.[4]Many investigators believe lipid abnormalities may contribute to renal damage by accelerating atherosclerosis, as well as intrarenal microvascular and macrovascular disease,

which could result in microalbuminuria. Some studies have also shown that hyperlipidemia may have a role in the progression of renal disease. [8]A substantial body of evidence supports the hypothesis that lipids may be involved in glomerulosclerosis and the progression of renal disease. The resemblance between glomerular mesangial cells and vascular smooth-muscle cells and the important role of the latter cells in the process of atherosclerosis suggest that accumulation of lipids in the mesangial cells may cause or accelerate glomerulosclerosis. The accumulation of lipids in mesangial cells or glomerular macrophages, along with collagen, laminin, and fibronectin, supports similarities between the process of atherosclerosis and glomerulosclerosis.[9]

Microalbuminuria, insulin resistance and hyperinsulinemia in hypertension

Several investigators have described the presence of insulin resistance and hyperinsulinemia in a substantial number of patients with essential hypertension, Ferrannini et al[10]showed reduced sensitivity to insulin in a group of adult nonobese subjects with moderate to severe essential hypertension. A direct correlation was present between insulin resistance or plasma insulin concentration and severity of hypertension. [10] In obese subjects, the decrease in blood pressure associated with an exercise training program was limited to hyperinsulinemic patients who , after the exercise program, had the greatest decrease in plasma insulin level.Several lines of evidence also suggest that hypertensive patients with hyperinsulinemia excrete greater amounts of urinary albumin. As in other forms of insulin resistance, it is possible that in patients with essential hypertension and microalbuminuria, the activation of glycogen synthase by insulin may be impaired.

Doria et.al[11] showed a significant correlation between UAE and insulin resistance in patients with essential hypertension, as well as in patients with type 2 diabetes mellitus. An association between insulin resistance and micro albuminuria has also been described by Falkner et.al[12] in young blacks. Microalbuminuria can be considered a manifestation of the metabolic derangements that predispose to NIDDM.

The significance of the association between insulin resistance and microalbuminuria is uncertain. Because microalbuminuria and insulin resistance[13] occur in nondiabetic normotensive subjects with genetic predisposition to hypertension, and hyperinsulinemia and insulin resistance are genetically transmitted, microalbuminuria and enhanced plasma insulin response to glucose could be both genetically determined and cosegregate with the hypertensive status. Alternatively, insulin resistance, hyperinsulinemia, or both could be causally related to microalbuminuria. Finally, enhanced plasma insulin response to glucose, insulin resistance, and microalbuminuria could be the consequence of hypertension.[14]

Insulin could directly or indirectly increase UAE through a variety of mechanisms. Insulin could lead to arteriosclerosis, renal damage, and microalbuminuria through its effects on blood pressure and lipid metabolism or through its trophic actions. The structure of an atherosclerotic plaque is characterized by excessive amounts of lipid and collagen, foam macrophages, and proliferation of smooth-muscle cells. In vitro, insulin can stimulate the proliferation of smooth muscle cells and collagen deposition through stimulation of growth-promoting

factors.[15] Insulin can increase cholesterol and triglyceride synthesis and enhance LDL receptor activity in arterial smooth-muscle cells, fibroblasts, andmononuclear cells. Insulin may alter glomerular hemodynamics directly or in association with such other factorsas catecholamines, angiotensin II, glucagon, and sodium.[16] It is worth mentioning that insulin may contribute to the salt sensitivity of blood pressure by causing sodium retention[17] or by activation of the sympathetic nervous system.Insulin could increase UAE by altering glomerular membrane permeability. A good estimate of vascular permeability to albumin can be obtained from the measurement of the albumin transcapillaryescape rate (TER). Patients with type 1,240 as well as type 2, diabetes mellitus2 [18]and microalbuminuria manifest greater albumin TERs than patients without microalbuminuria.

Hyperinsulinemia could contribute to microalbuminuria by altering endothelial function. Inpatients with essential hypertension and microalbuminuria, endothelial dysfunction could lead to both microalbuminuria and insulin resistance.

Microalbuminuri , Nephroangiosclerosis

In a study of mostly normotensive young adults (90%) performed by Jiang et al, a significant correlation was present between UAE and levels of blood pressure among blacks, but not among whites. The relationship occurred independent of age or body weight and was stronger in subjects with higher levels of blood pressure. This suggests microalbuminuria could be an early marker of renal damage.[19] In 88 previously untreated patients with hypertension, Schmieder et al observed that individuals with high creatinine clearance (indicating hyperfiltration) at baseline were more likely to show an increase in serum creatinine level after 7 years. After a follow-up of 5 years, Ruilope et al[20]reported a decline of 11 mL/min in creatinine clearance among 24 hypertensive patients with microalbuminuria as opposed to a decrease of only 2 mL/min in 49 hypertensive patients with normal UAE. In a retrospective cohort analysis of 141 hypertensive individuals followed up for approximately 7 years, it was observed that decrease in creatinine clearance was significantly greater in patients with microalbuminuria than in those with normal UAE (–12.1 _ 2.77 versus –7.1 _ 0.88 mL/min;*P* _ 0.05).271 These studies suggest that hypertensive individuals with microalbuminuria may experience a faster decline in renal function than patients with a normal UAE rate.

Effect of antihypertensive drugs on microalbuminuria

In patients with severe hypertension, reduction of blood pressure uniformly results in decreased UAE. De Venuto et.al[21] observed that captopril, not a calcium channel blocker, decreased UAE in patients with essential hypertension despite similar antihypertensive action. The greater antiproteinuric action of ACE inhibitors has been attributed to selective vasodilatation of the glomerular efferent arterioles and to a decrease in intraglomerular hydrostatic pressure. A direct effect of these drugs on the glomerular basement membrane permselectivity cannot be ruled out. It is noteworthy that alterations of intraglomerular pressure also affect the permeability of the glomerularbasement membrane. The antiproteinuric action of ACE inhibitors is potentiated by dietary salt restriction and reduced by high salt intake.[22]

The diabetes sub study of heart out comes

prevention evaluation (HOPE) study[23] (*n a*_ 3,577); showed that at similar blood pressure angiotensin converting enzyme inhibitor (ramipril) resulted in a 24.% greater reduction in the rate of progression to overt nephropathy than did the placebo in patients with type 2 diabetes mellitus and microalbuminuria or normoalbuminuria. (95% CI 3 to 40%; *P* _0.027) ACEI reduced albumin/creatinine ratio at 1 yr (*P* _ 0.001) and at study end (*P* _ 0.02).

In the irbesartan in patients with type 2 diabetes mellitus and microalbuminuria study (parving et al, 2001) treatment with irbesartan decreased the level of urinary albumin excretion by 38% from base line and over the period of three year follow up , reduced the risk of progression to macroalbuminuria by 70% as compared to placebo.[24]

The reduction of end points in NIDDM with the angiotensin II antagonist losarten (RENNAL) study[25]showed that as compared to th e conventional treatment alone(i.e without ACE inhibitor) losarten combined with conventional treatment decreased the level of protein excretion by35% and reduced the risk of end stage renal disease by 28%(Brenner et al,2001). It has been reported that the use of ACE inhibitor, leads to larger decrease in albuminuria when compared to other anti hypertensive eg amlodipine, chlorthalidone, doxazosin. In administration of losartan, or atenolol, was associated with the more decrease in albumin excretion with the losartan, within the similar range of blood pressure control.

In diabetic nephropathy, angiotensin converting-enzyme (ACE) inhibitors have a greater effect than other anti hypertensive drugs on proteinuria and the progressive decline in glomerular filtration rate (GFR).Whether this difference applies to progression of nondiabetic proteinuric nephropathies is not clear. The RamiprilEfficacy. In Nephropathy (REIN) study of chronic non diabetic nephropathies aimed to address whether glomerular protein traffic influences renal-disease progression, and whether an ACE inhibitor was superior to conventional treatment, with the same blood-pressure control, in reducing proteinuria, limiting GFR decline, and preventing end stage renal disease.[26]

In chronic nephropathies with proteinuria of 3 g or more per 24 hr, ramipril safely reduces proteinuria and the rate of GFR decline to an extent that seems exceed the reduction expected for the degree of blood pressure lowering. Randomised placebo controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy, The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia).[27]

In GISEN study a prospective double-blind trial, 352 patients were classified according to baseline proteinuria (stratum 1: 1–3 g/24 h; stratum 2: _3 g/24 h), and randomly assigned ramipril or placebo plus conventional antihypertensive therapy targeted at achieving diastolic blood pressure under 90 mm Hg. The primary endpoint was the rate of GFR decline. Analysis was by intention to treat.[27]

The results of the stratum 2 shows Urinary protein excretion significantly decreased ($p<0{\cdot}01$) by month 1 in the ramipril group, and remained lower than baseline throughout the study period. Compared with baseline, median percentage changes in urinary protein excretion were _23%, _35%, _23%,_33%, _50%, and _55% at 1, 3, 6, 12, 24, and

36months, respectively. Urinary protein excretion did not change significantly in the placebo group.The results of stratum 1, showed that: proteinuria decreased by 13% in ramipril group and increase by 15% in controls.[28]

In a study by Ruth Campbell and et al a prospective randomized cross over study of 24 patients with non diabetic chronic nephropathies , over 8 weeks ,has shown that at comparable blood pressure the combined ACEi and ARA decreased the proteinuria better than ACEi and ARA alone.(ACE inhibitor (benazepril) & ARB (valsartan) reduces proteinuria by 45.9% & 41.5%, respectively and half dose combined reduced proteinuria by 56%).[29]

In a study by the ATLANTIS study group, using the multicentric, randomized placebo controlled double blind study in 28 diabetics clinic in UK and Irerland, has shown that microalbuminuria is significantly reduced by ramipril treatment in type 1 diabetic patients without hypertension (P value 0.013) the proportion of patient progressing to macroalbuminuria was reduced in ramipril group. More patient on ramipril group regressed to normoalbuminuria(11% for ramipril 1.25mg, 20% for ramipril 5mg and 4% for placebo).[30]

MARVAL[31](MicroAlbuminuria Reduction With VALsartan) UAER at 24 wk was reduced by 44% with valsartan and 8% with amlodipine (p _ 0.001); valsartan significantly reversed MA to normal albuminuria in type diabetes mellitus (N=332).

INNOVATION [32](2007) (INcipieNt to OVert: Angiotensin IIreceptor blocker, Telmisartan, Investigation On type 2 diabetic Nephropathy) study showed that Transition rates to overt nephropathy were 16.7% with 80 mg telmisartan (n = 168), 22.6 with 40 mg telmisartan (n = 172), and 49.9% with placebo in Type 2 diabetes and UACR 100-300mg/g, (p _ 0.0001).

VIVALDI[33]2008 (investigate the effi cacy of telmIsartan versus VALsartan in hypertensive type 2 DIabetic patients with overt nephropathy) demonstrated Comparable reduction in 24 h urinary protein excretion rates. Geometric mean reduction (95% confidence interval) telmisartan, 33% (27%–39%); valsartan, 33% (27%–38%) in proteinuric type 2 diabetics.

The Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study (IRMA) - showed that irbesartan has a dose dependent improvement in time to onset of diabetic kidney disease.[24] After a follow up of 2 years, it was found that only 5.2% patients treated with irbesartan 300 mg progressed to overt nephropathy as opposed to 9.7% of those receiving irbesartan 150 mg and 14.9% of those receiving placebo. Similar observations reported in the Irbesartan type II Diabetic Nephropathy Trial (IDNT), showed that irbesartan was superior to both placebo and amlodipine in improving time to the primary endpoint, which was the composite of doubling of baseline serum creatinine and development of ESRD.

The Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan Study (RENAAL) study was similar to the IDNT and IRMA studies and demonstrated delayed time to onset of renal dysfunction in the losartan treated group.[25] Post hoc analyses of proteinuria as secondary endpoint showed that early response to losartan therapy is an important predictor of long term renal protection.

A comparison of telMisartan versus losArtan in hypertensive type 2 DiabEtic patients with Overt nephropathy (AMADEO) After one year of therapy with the two ARBs, telmisartan provided greater reductions in the amount of protein in the urine a finding not attributed to blood-pressure control, as reductions in SBP and DPB were similar in both treatment arms.[34]

DETAIL (The Diabetics Exposed to Telmisartan and EnalaprIL) study compare the effi cacy of long-acting telmisartan with ACE inhibitor enalapril.[35] Although there was an initial advantage in slowing down the decline in GFR with telmisartan, end of trial analyses could only demonstrate non-inferiority over enalapril .

BENEDICT (The Bergamo Nephrologic Diabetes Complications Trial)[36] demonstrated ACE inhibitor trandalopril significantly delay the development of microalbuminuria as compared to verapamil versus placebo.

n _ 37,089) that compared the effect of ACEI or ARB with that of other antihypertensive agents found that ACEI or ARB therapy was associated with reduction in risk for ESRD (risk reduction 0.87; 95% CI 0.75 to 0.99; *P* _ 0.04) ACEI or ARB therapy reduced daily albumin excretion in patients without diabetes (_15.73 mg/d; 95% CI _24.72 to _6.74; *P* _ 0.001; 44 trials; *n* _ 5,266) and in patients with diabetes (_12.21 mg/d; 95% CI _21.68 to _2.74).[33]

In ramipril efficacy in nephropathy study the decline in GFR per month was not significantly different (ramipril 0·26 [SE 0·05] mL per min per 1·73m^2, control 0·29 [0·06]). Progression to ESRF was significantly less common in the ramipril group (9/99 *vs* 18/87) for a relative risk (RR) of 2·72 (95% CI 1·22–6·08); so was

Interestingly, ONTARGET evaluated the use of ACE inhibitor in prevention of early chronic kidney disease.[37]RAAS control with ACE inhibitor has been shown to prevent the emergence of persistent microalbuminuria in patients with type 2 diabetes and apparently normal urinary albumin levels (_20 □g/min).

ONTARGET[37] (ONgoing Telmisartan Aloneand in combination with Ramipril Global Endpoint) A Study done on 55 years or older with established atherosclerotic vascular disease or with diabetes with end-organ damage (n= 8542) to evaluate primary outcome Composite of dialysis, doubling of CR, and death demonstrated that outcome was similar for telmisartan (1147 [13.4%]) and ramipril (1150 [13.5%]; HR 1.00, 95% CI 0.92-1.09), but was increased with combination therapy (1233 [14.5%]; HR 1.09, 1.01-1.18, p = 0.037).

A meta-analysis of 13 trials (

progression to overt proteinuria (15/99 vs 27/87, RR 2·40 [1·27–4·52]). In parallel, stratum 1 had almost a threefold slower □GFR than stratum 2 (0·27 [0·04] mL/min per month *vs* 0·72 [0·08] mL/min per month, p=0·0001). When the REIN core study was concluded, eight (4·3%) of the 186 patients in stratum 1 and 34 (20·5%) of the 166 patients in stratum 2 had progressed to ESRF. Stratum 1 had almost a fivefold lower incidence of ESRF than stratum 2 (RR 5·44 [95% CI 2·52–11·64], p=0·0001).

DETAIL[35]2004 Type 2 diabetes with early nephropathy 250 Telmisartan/enalapril Change in the GFR (determined by measuring the plasma clearance of iohexol) Change in the GFR was -17.9 mL/min/1.73 m2 of body surface area with telmisartan, as compared with -14.9 mL/min/1.73 m2 with enalapril, for a

treatment difference of -3.0 mL/min/1.73 m2 (95 % CI -7.6–1.6 mL/ min/1.73 m2).

Conclusion:

Microalbuminuria appears early and is the most important risk for progressive kidney disease. Hypertension accelerates the progressive increase in albuminuria and decline in glomerular filtration. Greater urinary albumin excretion is due to increased glomerular hydrostatic pressure and increased permselectivity of the glomerular basement membrane.. Reduction in albuminuria is protective for the development of end stage renal disease, coronary artery disease and cerebrovascular disease.. In a study proteinuria decreased by 13% in ramipril therapy in patients having proteinuria of 1–3 g/24 h and among those having proteinuria of >3 g/24 median percentage decrease in urinary protein excretion were 23%, 35%, 23%,33%, 50%, and 55% at 1, 3, 6, 12, 24, and 36months, respectively. A meta-analysis of 13 trials (*n* _ 37,089) found that ACEI or ARB therapy reduced daily albumin excretion and is associated with reduction in risk for ESRD (risk reduction 0.87; 95% CI). The use of Angiotensin converting enzyme inhibitor or angiotensin receptor blocker leads to larger reduction in albuminuria and decerease the progression of chronic kidney disease.

References:

1. Kannel WB, Stampfer M William P. Castelli M, Joel V. The prognostic significance of proteinuria: The Framingham Study. Am Heart , 1984;108:1347-1352
2. Gerber LM, Shmukler C, Alderman MH: Differences in urinary albumin excretion rate between normotensive and hypertensive white and nonwhite subjects. Arch Intern Med 1992; 152:373-377
3. **Edwards RM:** Segmental effects of norepinephrine and angiotensin II on isolated renal microvessels. Am J Physiol 1983;244:F526-F534
4. **Raij L, Chiou X, Owens R, Wrigley B:** Therapeutic implication of hypertension-induced glomerular injury:Comparison of enalapril,combinationofhydralazinereserpine -hydrochlorothiazide. Am J Med 1985;9:37-41
5. **Hostetter TH, Olson JL, Rennke HG, Venkatachalam MA, Brenner BM:** Hyperfiltration in remnant nephrons: A potential adverse response to renal ablation. Am J Physiol 1981241:F85-F93
6. **Campese VM:** Salt-sensitivity in hypertension. Renal and cardiovascular implications. Hypertension 1994;23:53 550
7. **van Hooft IMS, Grobbee DE, Derkx FHM, de Leeuw PW, Schalekamp ADH, Hofman A:** Renal hemodynamics and the renin-angiotensin-aldosterone system in normotensive subjects with hypertensive and normotensive parents. N Engl J Med 1991;324:1305-1311
8. **Keane WF:** Lipids and the kidney. Kidney Int 1994;46:910- 920
9. **Pai R, Kirschenbaum MA, Kamanna VS:** Low density lipoprotein stimulates the expression of macrophage colony-stimulating factor in glomerular mesangial cells. Kidney Int 1995;48:1254-1262
10. Ferrannini E, Buzzigoli G, Bonadonna R, GioricoMA, Oleggini M, Graziadei L, Pedrinelli R, Brandi L, Bevilacqua S: Insulin resistance in essential hypertension. N Engl J Med1987; 317:350-357
11. Doria A, Fioretto P, Avogaro A, Carraro A, Morocutti A, Trevisan R, Frigato F, Crepaldi G, Viberti GC, Nosadini R: Insulin resistance is associated with high sodiumlithium countertransport in essential hypertension Am J Physiol 1991;261:684-691
12. Falkner B, Kushner H, Levison S, Canessa M: Albuminuria in association with insulin and sodium-lithium countertransport in young African Americans with borderline

hypertension. Hypertension 1995;25:1315-1321

13. Ferrari P,Weidmann P, Shaw S, Giachino D, Riesen W, Alleman Y, Heynen G: Altered insulin sensitivity, hyperinsulinemia, and dyslipidemia in individuals with a hypertensive parent.Am J Med1991; 91:589-596

14. Falkner B, Hulmans S, Tannembaum J, Kushner H: Insulin resistance in young black men. Hypertension 1990;16:706- 711

15. Stout RW, Bierman EL, Ross A: Effect of insulin on the proliferation of cultured pri Nakao J, Ito H, Kanayasu T, Murota SI: Stimulatory effect of insulin on aortic smooth muscle cell migration induced by 12-L-hydroxy 5,8,10,14 eicosatetraenoic acic and its modulation by elevated extracellular glucose levels. Diabetes 1985;34:185-191

16. Sholey JW, MeyerTW: Control of glomerular hypertension by insulin administration in diabetic rats. J Clin Invest 1989;83:1384-1389

17. DeFronzo RA, Cooke CR, Andres R, Faloona GR, David PJ: The effect of insulin on renal handling of sodium, potassium, calcium, and phosphate in man. J Clin Invest 1975;55:845-855

18. Nannipieri M, Rizzo L, Rapuano A, Pilo A, Penno G, Navalesi R: Increased transcapillary escape of albumin in microalbuminuric type II diabetic patients. Diabetes Care 1995; 18:1-9

19. Jiang X, Srinivasan SR, Radhakrishnamurthy B, Dalferes ER, Bao W, Berenson JS: Microalbuminuria in young adults related to blood pressure in a biracial (blackwhite) population. The Bogalusa Heart Study. Am J Hypertens 1994; 7:794-800

20. Ruilope LM, Campo C, Rodriguez-Artalejo F, Lahera V, Garcia Robles R, Rodicio JL: Blood pressure and renal function: Therapeutic implications. J Hypertens 1996;14: 1259-1263

21. De Venuto G, Andreotti C, Mattarei M, Pegoretti G: Long-term captopril therapy at low doses reduces albumin excretion in patients with essential hypertension and no sign of renal impairment. J Hypertens 1985;3:S143-S145, (suppl 2)

22. Heeg JE, DeJong PE, van der Hem GK, de Zeeuw D: Reduction of proteinuria by converting enzyme inhibition. Kidney Int 1989;36:272-279

23. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-convertingenzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators(HOPE). *N Engl J Med.* 2000;342(3):145–153.

24. Parving H, Lehnert H, Arner P, et al. Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study Group The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med*. 2001;345(12):870–878.

25. Brenner B, Cooper M, Zeeuw D, et al. RENAAL Study Investigators. Losartan in

patients with type 2 diabetes and proteinuria: Observations from the RENAAL Study. *N Engl J Med*. 2001; 345(12):861–869

26. Piero R. Perna A. Remuzzi G. ACE Inhibitors to Prevent End-Stage Renal Disease: When Start and Why Possibly Never to Stop: A *Post Hoc* Analysis of the REIN Trial Results .J Am Soc Nephrology 2001; 12: 2832–2837

27. Piero R, Eva P, Luciana T, Roberto R, Livio G, Giuseppe R(GISEN GROUP). Ramipril prolongs life and is cost effective in chronic proteinuric nephropathy" kidney international 2001;vol.59:pp 286-294

28. Piero Ruggenenti, annalisa perna,et.al Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy, Lancet1997; 349: 1857–63

29. Ruth C., Fabio S. et al 'the effects of combined ACE inhibitor and angiotensin II antagonist treatment in human chronic nephropathies', kidney international,vol 63 ,2003 : 1094-1103

30. J.P O Hare, R Bilous et.al (ATLANTIS group)'low dose ramipril reduces Miroalbuminuria in Type 1 Diabetic patients

without Hypertension', Diabetes care 2000;Vol 23,no.12

31. Viberti G, Wheeldon NM, et al. MicroAlbuminuria Reduction With VALsartan (MARVAL) Study Investigators. Microalbuminuria reduction with valsartan in patients with type 2 diabetes mellitus: a blood pressure-independent effect. *Circulation*. 2002;106:672–678. 2005;25(1):41–46
32. Makino H, Haneda M, Babazono T, et al. The Telmisartan Renoprotective Study from Incipient Nephropathy to Overt Nephropathy – Rationale, Study Design, Treatment Plan and Baseline Characteristics of the Incipient to Overt: Angiotensin II Receptor Blocker, Telmisartan, Investigation on Type 2 Diabetic Nephropathy (INNOVATION) Study.*J Int Med Res*. 2005;33:677–686.
33. Galle J, Schwedhelm E, Pinnetti S, et al. VIVALDI investigators. Antiproteinuric effects of angiotensin receptor blockers: telmisartan versus valsartan in hypertensive patients with type 2 diabetes mellitus and overt nephropathy. *Nephrol Dial Transplant*. 008; 23(10):3174–3183.
34. Bichu P.,Nistala.Khan A. Sowers J.Angiotensin receptor Blockers for the reduction of proteinuria in diabetic patients with overt nephropathy : AMADO study Vascular Health and Risk Management 2009:5
35. Barnett AH, Bain SC, Bouter P, et al. Diabetics Exposed to Telmisartan and Enalapril Study Group. Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy. *N Engl J Med*. 2004;351(19):1952–1961
36. M, Ruggenenti P, et al. Prevention and treatment of diabetic renal disease in type 2 diabetes: the BENEDICT study. *J Am Soc Nephrol*. 2006;17(4 Suppl 2):S90–S97.
37. Mann JF, Schmieder RE, McQueen M, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomized, double-blind, controlled trial. *Lancet.* 2008; 372(9638):547–553

Correspondence Address: **Mahesh Bhattarai**, Lecturer Department of Internal Medicine, Nobel Medical College and Teaching Hospital, Biratnagar. ***Address of Correspondance:*** **Buna Bhandari**, Lecturer, Department of Community Medicine, Nobel Medical College and Teaching Hospital, Biratnagar.

EFFICACY OF SINGLE DOSE OF 800µg OF MISOPROSTOL IN FIRST TRIMESTER ABORTION

Shanti Subedi

Abstract:

Objective: To assess the efficacy, safety and cost effectiveness of Misoprostol (Prostaglandin E1 analogue) as a single dose of 800µg in first trimester abortion
Methods: A descriptive study was conducted in Nobel Medical College and Teaching Hospital from June 2010-June 2011 where 110 patients were enrolled for first trimester abortions including incomplete, missed, blighted ovum. Each woman received a single dose of 800µg of Misoprostol intravaginally and the the process of abortion was monitored to assess the outcome measures.
Results: Successful abortion was seen in 102 patients (92.7%) with induction to delivery interval of < 24 hours and the remaining 8 (7.2%) of them had to undergo surgical evacuation. Side effects noted were lower abdominal pain, fever, nausea, vomiting, and diarrhoea. Mean hospital stay of the patients was 48 hours.
Conclusion: Misoprostol is a safe, cost effective and efficacious drug for first trimester abortion even as a single dosage.

Key words: *Misoprostol, abortion, uterine curettage*

Introduction:

Termination of pregnancy for various maternal as well as foetal indications is a common problem. The rate of maternal mortality and morbidity increases significantly by surgical methods for termination of pregnancy as compared to medical means.

Misoprostol, Prostaglandin E1 analogue was previously widely used for prevention and treatment of gastric ulcers and now an important drug for women's reproductive health. An increasing body of literature has shown that it can be used as labour induction and it also holds promise for other indications like cervical ripening, treatment and prevention of postpartum haemorrhage and treatment of spontaneous abortion. Finally there is a growing body of literature on misoprostol for its widespread use for termination of first trimester abortion. Several studies have already been done to prove its efficacy till date.[1,2]

Misoprostol is an appealing candidate as a medical method of early as well as second trimester abortion.[3,4] It is available in many countries and very cost effective, easy to administer with minimal side effects. As the author could not find any such prototype study that might have explain the efficacy of Misoprostol among the female population living in eastern part of Nepal, this project is conducted with an objective to fulfil this lacunae.

Materials and methods:

This study was conducted in NMCTH from June2010-June 2011 where 110 patients were enrolled for first trimester abortion. A total of 110 patients with medical indications of abortion were included. Only inclusion criteria was

hemodynamically stable first trimester abortion and exclusion criteria were-

1. Signs of pelvic infection and sepsis.
2. Cardiovascular disease
3. Bronchial Asthma
4. Known allergy to misoprostol and other prostaglandin
5. Hemodynamically unstable
6. Patients unable to give consents.

Subjects fulfilling the inclusive criteria were admitted in the labour ward of the hospital. After a detail interview and physical examination 800µg of misoprostol was administered to them intravaginally. Vigilant monitoring of the patient was done to avoid any of the complications.

The primary outcome measure was the successful abortion within 48 hours and the other outcome were induction to delivery interval, its complications and need for surgical evacuation. Surgical evacuation was needed in those with incomplete expulsion, excessive vaginal bleeding and it was done under paracervical block.

All the patient were kept in the hospital for at least 48 hours to assess the response and if they don't expelled the products of conception within that period, sonography was done after 2 weeks and uterine curettage performed if any retained products found.

In the case of heavy bleeding during the treatment 8 out of all enrolled in the study cases underwent curettage immediately but none of them required blood transfusion.

Results and Discussion:

In this study the successful abortion rate was 92.7% that too with a single dosage regimen intravaginally and this figure is higher than the figure reported by Fiala and Weeks, who reported a success rate of 87.5% with multiple dosages[5]. Success rate of 91.3% has been reported in a study done in tertiary centre of Nepal but that was combined with Mifepristone and the gestational age was only of 56 days[6]. Dose in this study was 400µg orally. Several clinical trials have evaluated the use of misoprostol alone for early pregnancy failure.[7,8,9,10]

The success rate reported in the most of them 60-90% depending on the dose, mode and frequency of drug administration. A study reported by Szymanska et.al in 2003 had a success rate of only 30.3% but the dose they have used was only 400µg[11]. Another study done by Thomas Betsy et al reported a success rate of 71.7% after a single dose and 76.7% after two doses, thus they were using 800ug but in divided doses[12]. Success rate of 62% was observed by Sedigheh et al in 2008 with 800µg vaginally and success of 34% with second dose[1].

Conclusion:

Misoprostol is safe, cost effective and efficacious drug even as a single dose for first trimester abortion.

References:

1. **Sedigheh A, Fatemeh R, Naiereh K, and Mohamed S**. *Medical abortion at first trimester of pregnancy with misoprostol*. Saudi Med J. 2008; Dec: 29(12), 1739-1742.

2. **Bhattacharjee N, Saha SP, Ghoshroy SC, Bhowmik S, and Barui G**. *A randomized comparative study on sublingual versus vaginal administration of misoprostol for termination of pregnancy between 13-20 wks*. Aust NZJ. Obstet Gynaecol. 2008; April; 48(2):165-71.
3. **Blanchard K, Winikoff B, Kurus C, Nguyen T, and Nhu N**. *Misoprostol Alone- A new*

method of medical abortion? Contraception. 1999: 59, 209-217

4. **Blanchard K, Winikoff B, and Ellertson C**. *Misoprostol use alone for the termination of early pregnancy. A review of the evidence*. Contraception. 1999: 59, 209-217

5. Fiala C and Weeks A. *Misoprostol Dosage guidelines for Obstetrics and Gynecology*. 2005; 2-8

6. **Karki C and Pokahrel H**. *Acceptibility and feasibility of medical abortion in Nepal*. Int J. Gynaecol Obstet. 2009: Jul; 106 (1), 39-42

7. **Jain JK, Harwood KR, Meckstoth, DR, and Mishell**. Early pregnancy termination with vaginal misoprostol combined with loperamide and acetaminophen prophylaxis. Contraception. 2001: 63; 217-221.

8. **Wood, SL and Brain PH**. *Medical management of missed abortion;* A Randomised Controlled trial, Obstet. Gynecol. 2002: 99; 563-566

9. **Prasartsakulchai, C and Tannirandorn YA.** *Comparison of Vaginal misoprostol 800ug versus 400ug in rearly pregnancy failure: A Randomised Controlled tria*l. J. Med. Assoc.Thai. 200: 487,518-523.

10. **Carbonell JLL, Velarco A, and Fernandez C**. *The use of misoprostol for termination of early pregnancy*. Contraception. 1997: 55, 165-168

11. **Szymanska, M. Suchonska, B. Ziolkowaska and L. Bablok**, *Use of misoprostol in the termination of missed abortion*. Med. Wieku. Rozwoj. 2003: 307-317

12. **Thomas B and Habeebullah S**. *Vaginal Misoprostol for Medical evacuation of early pregnancy failure*. J Obstet Gynecol Ind. 2004: 54: 340-342.

Correspondence Address: **Dr.Shanti Subedi**: Lecturer, Department of Gynaecology and Obstetrics, Nobel Medical College and Teaching Hospital, Biratnagar. ***Address of correspondence*****: Dr.Shanti Subedi**, Lecturer, Department of Genecology and Obstetrics, NMCTH, Biratnagar. Phone no-9842021806.E-mail-drshantisubedi@yahoo.com

UPREGULATION OF CYCLOOXYGENASE SYSTEM AND GROWTH FACTORS AS PLAUSABLE MECHANISM OF ANTINUCLEROGENIC ACTIVITY OF LEAF OF *PIPER BETLE* Linn: A MOLECULAR INSIGHT

Biswajit Majumdar, Amar Kumar Sinha, Shekhar Chandra Yadav, And Dilli Ram Niroula

Abstract:

Allylpyrocatechol, the active component obtained from ethanol extract of leaves of Piper betle Linn *at a dose of 120mg/kg body weight was shown to be an antiulcerogenic agent . Allylpyrocatechol was isolated from PBE by column chromatographic separation followed by preparative TLC and tested in rat ulcer model. Histological studies reveal that damage in the mucosal epithelium was corrected and the disrupted epithelium (as seen in ulcer) reversed with the test compound. The cellular, molecular and biochemical factors underlying the healing of gastric ulcer, such as, growth factors (EGF, EGF-R, SMAD-4) and cyclooxygenases (COX-1 and COX-2) were observed to be up-regulated in presence of APC during healing process. All the data showed statistical significance (by one way ANOVA) when compared to the experimental control value.*

Key words: *Allylpyrocatechol, COX-1,2; EGF/EGF-R, Gastric ulcer, Piper betle Linn.*

Introduction:

Gastric ulcer is a disease, very common worldwide. Apart from the major causative agent, *H.pylori*, the spiral bacteria, the next common cause of induction of gastric ulcer are the NSAIDs (Non-steroidal anti-inflammatory drugs), which are very commonly taken by the people as pain-killers. The NSAIDs induce ulcer by several mechanisms, one being the involvement of free radicals by neutrophil activation. The free radical damage occurs mainly by the lipid peroxidation. There has been an accumulative evidence of the involvement of prostaglandin, cyclooxygenase 1 & 2, Nitric oxide, inducible Nitric oxide synthatase and different cytokines are induced or increased by gastric ulceration and might also contribute ulcer healing. There is a cross-over role of COX-1 and COX-2 with inflammatory process and ulcer healing. It is reported that several growth factors, when up- regulated, enhance the healing process of ulcer. The most widely involved growth factors being Epidermal Growth Factor (EGF), its receptor (EGF-R) and the components of TGF-pathway (eg. SMAD-4). Numbers of synthetic drugs are available in the market and are effectively used to cure NSAID-induced gastric ulcer, but all of them are reported to have several side effects. The most widely used drug, being, Misoprostol, is reported to produce diarrhea, nausea, vomiting etc. It's even not permissible for pregnant women, as Misoprostol has an abortive property. Hence, the need for a safer drug to combat against NSAID-induced gastric ulcer is yet not fulfilled that limits the usage of NSAID. Plant drugs are normally known to have lesser or no side-effects. The plant-parts,

which are already edible to people are even expected to be non-toxic. Hence, the ultimate finding of a drug from plant origin, which can heal the NSAID-induced gastric ulcer, enhance the COX iso-forms and the express the up-regulation of the Growth factors can lead to the development of a drug with better prospect and accessible to the common people.

Materials and Methods:

Extraction of Plant part in Suitable Solvent:

Fresh leaves (P. betle) 250 gm was dissolved in 1L of 95% alcohol or 1L of Ethyl Alcohol (as specified before) at 4oC x 7 days with change and intermittent shaking. Filter through nylon cloth. The pooled filtrate is put in the rotary evaporator under vacuum and the extract, devoid of organic solvent was isolated. It was lyophilised under pressure, to remove water content and stored at vacuum (PBE= P. betle Ethanolic extract)

Isolation of compounds from PBE:

1.71 g of PBE and 50ml ethanol was filtered and the filtrate treated with activated charcoal(0.1g)and allowed to stand overnight(to get rid of the chlorophyll pigment, filtered, concentrated in vacuum , when a dark brown sticky mass was obtained.(1.038g) (hence, 60.7% yield).0.5g of this was subjected to column chromatography over a silica gel column containing 5g of silica gel and eluted with 10% methanol-chloroform and 5 fractions were collected (~50ml each).

Fraction 1-Concentrated in vacuum and put to preparative TLC on a silica gel plate, using 5% EtOAc-Hexane as the solvent. The TLC band at Rf 0.7 was scrapped from the plate and eluted with chloroform. Concentration in vacuum furnished a pure compound (8.4mg), which was identified as Chevibetol by IR and 1H NMR Spectroscopy. (The compound was already reported.)

Fraction 2- Concentrated in vacuum and subjected to preparative TLC using 5% methanol- chloroform as solvent. It showed a major band with a polymeric material which gave colouration with FeCl3 spary, indicating its polyphenolic nature. Multiple developments of the TLC plate using same solvent resolved the major band into 2 closely spaced bands with Rf 0.3 and 0.35 respectively. They were scrapped and eluted with 20% methanol-chloroform. On concentration 2 compounds were obtained (49.2mg and 25.3mg respectively). The former was found to be Chevicol or Allylpyrocatechol, whereas, the latter, was shown to be unstable and gets oxidized very quickly. Spectral data showed that this compound was not reported earlier.

Fraction 4 and 5- on concentration gave 340.8mg and 73.0mg residues respectively. Positive Molisch test showed their Glycosidic nature. They didn't show any antioxidant property, Hence, no further study with them was done. Allylpyrocatechol was designated as P1 in our study.

Preparation of Drug from Different Extract:

The dose of the extracts to be given to the Rats of the experimental ulcer model, are standardized. The different standardized dosages are: PBE= 120mg/kg BW. The active fractions are given at a dose just similar to their percentage yields from the extracts. Hence the dose of P1 is selected as followed: P1=2.0 mg/kg BW.
All of them are mixed with 2% Gum Acacia, which works as a binder and reported to be a non-toxic one. The extracts are prepared in

distilled water as the solvent and are given by oral intubation to the Rats, using feeding cannulae 1 ml. of the prepared drugs are given each day.

Experimental Ulcer Model:

Under healing: Design of experiment: Rats: (Male Wister strain, male, wt 100-120 g.)

Group A	Group B	Group C	Group D
(5 Rats)	(5 Rats)	(15 Rats)	(15 Rats)

1ml of Vehicle (2% gum acacia) x 10 days, sacrificed (Normal control)

Indomethacin 30 mg/kg body wt. Overnight fasting, water adlibtium

Group B	Group C	Group D
(5 Rats)	(15 Rats)	(15 Rats)
Fasting overnight Sacrificed 4Hours	without drug (extractive) only vehicle	Treated with Drugs (2%Gum in 2%Gum Acacia After Indomethacin Administration acacia, 1ml) At pre-determined doses.
(Experimental Control)	(Experimental) Sacrificed on 7th day	

Quantification of Mucosal Injury:

The area of mucosal damage was calculated in square millimeters and expressed as percentage of the glandular stomach according to Szabo et.al.

Preparation of Tissue Homogenate:

Rat: Stomach tissue after the weight was homogenized using a glass Teflon homogenizing tube in 50mM phosphate Saline Buffer, pH 7.2 under cold condition. The homogenate was centrifuged at 2000 rpm for 10min and the supernatant, collected for Biochemical analysis.

Total Protein:

Total protein is estimated by the method of Lowry et al. Briefly, samples and standards (1mg/ml BSA in double distilled water) in different tubes are treated with 5ml of RA mixture (4.8% Na-K-Tartarate, 2% CuSO4 and 3% Na2CO3 in 0.1N NaOH at a ratio of 1:1:48 by volume). Then Phenol regent (half diluted double distilled water) is added to the reaction mixture with continual vortexing. The reaction mixture is allowed to stand for 30 minutes at room temperature and optical density is measured at 710nm using water as reagent blank.

Estimation of Lipid Peroxidation:

Lipid peroxidation in the ulcer tissue was measured by quantification of the Thio-barbituric acid reactive substances produced in the tissue. The method is as discussed earlier (261).

Histology of Gastric Mucosal Tissue:

Histopathological examination of gastric tissue was done as per the method described by Bancroft et al (275). The gastric tissue was immediately fixed in 10% buffered formal saline for 24 hours.

1. Tissue was washed in tap water.
2. Kept in 70% alcohol for 24 hours
3. Transferred to 90% alcohol for 24 hours.
4. Dehydrated in absolute alcohol- 3 changes for ½ hour each.
5. Put in Xylol for clearing- 3 changes for 15 minutes each.
6. Put in molten paraffin (fresh) (60°C-62°C).
7. Blocked by fresh molten paraffin. Each block was numbered.
8. The sections were cut with a Microtome with a thickness of 3-5 cm.
9. The ribbons of sections were floated Immediately in slides containing a drop of warm distilled water and the wrinkles were removed by teasing with a needle. Slides were placed on hot plate, so that the water evaporates, paraffin melts and the sections get fixed on the slides.

HaematoxylinE and Eosin Staining Solutions:

Harris' Method (Harris' Alum Haematoxylene):

a) Haematoxylene: Haematoxylene (5g); Absolute Alcohol (50cc); Ammonium/Potassium Alum (100g); Distilled Water(1000cc); Mercuric Oxide (2.5g); Glacial Acetic Acid (20cc);100g of Potassium Alum was dissolved in 100cc of warm Distilled water. 5g of Haematoxylene was dissolved in 50cc Absolute Alcohol. This mixture was added to the first mixture and brought to boil rapidly. Then 2.5g of mercuric oxide was added. The whole mixture was cooled rapidly by plunging the flask into cold

water. When the solution was cooled, 20 ml of Glacial acetic acid was added. The stain was filtered before using.

b) Eosin: Eosin Y (2mg); Distilled Water (100ml); 1mg of Eosin Y was dissolved in 100ml of distilled water. Thymol was added to inhibit fungal growth.

Procedure:

The sections were de-paraffinized after warming on hot tray for 2-3 minutes. The slides were put in Xylene for 20 minutes. They were hydrated through different grades of alcohol (100%, 90%, 70%, 50%, and 30%). Finally; they were kept in distilled water for 10 minutes. Haematoxylene stain was added and kept for 5 minutes. Slides were washed under running tap water for 15 minutes. Slides were passed through Alcohol gradation (30%, 50%, and 70%).Eosin was added and kept for 2 minutes. Slides were kept in 90% alcohol for 5 minutes. Slides were kept in 100% alcohol for 5 minutes and finally they were kept in Xylene for 30 minutes. Mounted in DPX.

Results: Nuclei Blue Black; Cytoplasm varying shades of Pink.

Estimation of COX-1 and –2, i-NOS, IL-8RA (CXCR1), Epidermal Growth Factor and Smad- 4 Protein:

Immunohistochemistry:

Mucosal specimen were deparaffinized in Xylene followed by 100% Alcohol. Kept in Methanol+H2O2 solution (200:1) for ½ hour. Washed in running tap water. Kept in PBS(pH 7.6) for 10 minutes. Slides were wiped and incubated with Blocking solution (Normal Rabbit Serum, 1:5 in PBS).Incubated with Primary antibody [Cox-1(1:50); Cox-2,IL-8RA, Smad-4, EGF-R(1:100) in PBS] for 1 hour. Washed in PBS. Incubated with secondary antibody HRP-labeled [1:500 anti-mouse IgG (for Cox-1, Cox-2, Smad-4); 1:500 anti-goat IgG (for IL-8RA); 1:500 anti-sheep IgG (for EGF-R)] for 1 hour. Washed in PBS.DAB (Diamino benzidine) solution was added and kept for 40 seconds. Washed in running water. Counterstained with Haematoxylene for 2 minutes. Washed in running water. Kept in 100% alcohol for 30 minutes. Kept in Xylene for overnight. Mounted in DPX.

Immunofluorescence:

Mucosal specimen were deparaffinized in Xylene followed by 100% Alcohol. Kept in 4% p-Formaldehyed. Washed in PBS (pH 7.6) for 10 minutes. Kept in Triton-X for 5 minutes. Slides were washed and incubated with Blocking solution (Normal Rabbit Serum, 1:5 in PBS).Incubated with Primary antibody [EGF-R(1:100) in PBS] for 1 hour. Washed in PBS. Incubated with secondary antibody FITC-labeled [1:500 anti-sheep IgG] for 1 hour. Washed in PBS. Mounted in DPX.

Polymerase Chain reaction:

RNA extraction and RT-PCR analysis: Total RNA was isolated by TRIzol method (Invitrogen) according to the manufacturer's protocol. 1 □g of RNA treated with RNase-OUT ribonuclease inhibitor (Invitrogen) was used for cDNA synthesis. Reverse-transcription using Superscript reverse transcriptase-II (Invitrogen) and Oligo dT (Invitrogen), to prime the reaction was carried out. PCR primers were selected to distinguish between cDNA and genomic DNA by using individual primers specific for different exons. 1 □l of cDNA was amplified by polymerase chain reaction

using Abgene 2X PCR master mix (Abgene, UK) and appropriate primers (Refer table M2). The expression of genes such as EGF and SMAD-4were checked. For all the genes, PCR were performed for 35 cycles, consisting of an initial denaturation at 94o C for 1 min, then 94o C for 30 sec, annealing temperature of the respective gene primer for 45 sec, 72o C for 1 min and was terminated by final extension at 72o C for 5 minutes.

Table 1: sequences of primers used in RT-PCR analysis.

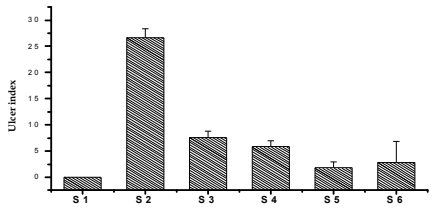
Genes	Primer Sequences
EGFR-F	AAGGATGTGAAGTGTGG
EGFR-R	ACTTTCTCACCTTCTGG
Smad4-F	AAGGTGGGGAAAGTGAAAC
Smad4-R	ATGCTTTAGTTCATTCTTGTG

Statistical tests by ANOVA.

The data generated from the different set of experiments were evaluated statistically using ANOVA, to determine the significance of Mean+SEM values. Differences were considered significant at $p<0.05$.

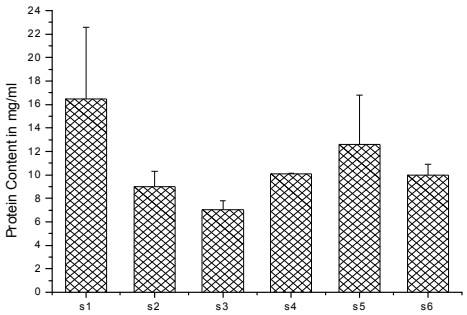
Results:

1. Ulcer index:



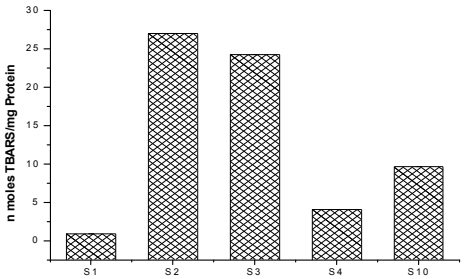
S1= Normal Rat Stomach; S2= 0th Day Ulcer Rat Stomach; S3= 7th Day Ulcer Rat Stomach (without treatment) S4= 7th Day Ulcer Rat Stomach (treated with PBE) ;S5= 7th Day Ulcer Rat Stomach (treated with P1) S6= 7th Day Ulcer Rat Stomach (treated with Misoprostol)

2. Total Protein



S1= Normal Rat Stomach ; S2= 0th Day Ulcer Rat Stomach ; S3= 7th Day Ulcer Rat Stomach (without treatment) S4= 7th Day Ulcer Rat Stomach (treated with PBE) ; S5= 7th Day Ulcer Rat Stomach (treated with P1) S6= 7th Day Ulcer Rat Stomach (treated with Misoprostol)

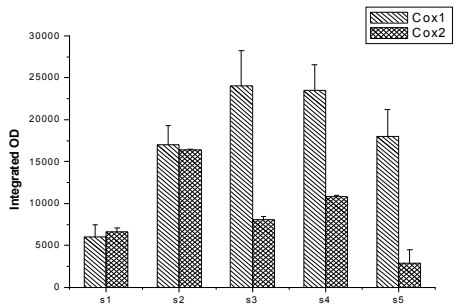
3. Lipid Peroxidation



S1= Normal Rat Stomach;S2= 0th Day Ulcer Rat Stomach;S3= 7th Day Ulcer Rat Stomach(without treatment) S4= 7th Day Ulcer Rat Stomach (treated with P1); S5=7th Day Ulcer Rat Stomach (treated with Misoprostol)

4. Immunohistochemistry of COX-1 and COX-2

COX-1 and COX-2 are two important factors in the induction of gastric ulcer. Though controversial, but generally it is known that COX-1 gets suppressed by the non-selective NSAIDs, forming gastric ulcer. COX-2 also gets lowered down. But in case of healing COX-1 level increases along with COX-2.



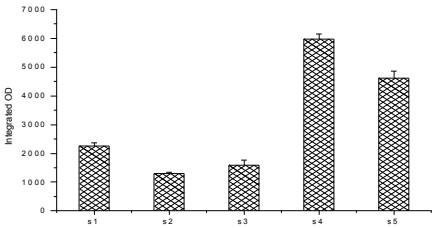
S1= Normal Rat Stomach;S2= 0th Day Ulcer Rat Stomach;S3= 7th Day Ulcer Rat Stomach (without treatment) S4= 7th Day Ulcer Rat Stomach (treated with P1); S5=7th Day Ulcer Rat Stomach (treated with Misoprostol)

Immunohistological data showed that COX-2 level lowers down at the onset of ulcer induction. In the 7th day ulcerated tissue, the COX-2 gets increased but the COX-1 still remains suppressed, showing ulcerated condition, as it is known that suppression of COX-1 leads to ulcer formation. But with the extracts the COX-1 as well as COX-2 level rises. The increase in COX-1 level is much more than the rise in COX-2. The results showed that P1 is effective in increasing the level of both COX-1 and COX-2.

5.Estimation of EGF, EGF-R:

Epidermal Growth Factor is an important factor in promoting the healing effect of gastric ulcer. In a normal tissue this protein is not very significant in amount but, whenever there is an ulcer formation, the protein gets synthesized in a large amount. A good healing agent should promote the synthesis of this protein as it helps in cell division and growth of new healthy cells which replace the disrupted ones.

a. By ELISA: ELISA is a standard method to measure the binding of antibody to EGF antigen. It is quick and easy method, hence, the binding of anti-EGF antibody can prove the presence of EGF in the tissue sample.

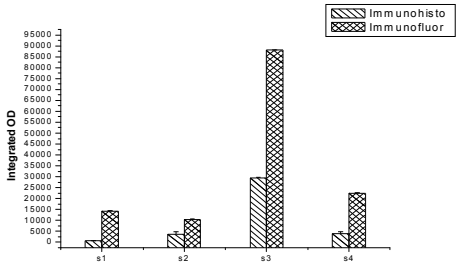


The ELISA shows large amount of EGF in the 0th day ulcerated tissue but without any treatment the 7th day ulcer tissue showed a decrease in the EGF amount, whereas, PI showed increase in the EGF amount, suggesting the quick healing procedure, as EGF enhances the healing.

b) Estimation of EGF-R by Immunohistochemistry and Immunofluorescence:

Since, Immunohistochemistry and Immunofluorescence are two important method in showing the binding of EGF-R molecule in the gastric epidermis, they are done and the colour developed by them are measured by a software, Biovis, which measures the amount of binding by measuring the Integrated OD against the binding in percentage area of the slide. The rise in Integrated OD is a measure of high

binding of the antibody.



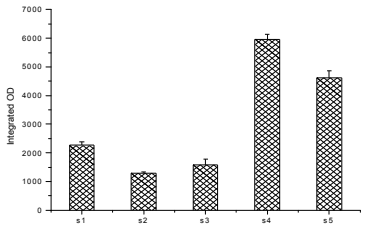
S1= 0th Day Ulcer Rat Stomach;S2= 7th Day Ulcer Rat Stomach(without treatment);S3= 7th Day Ulcer Rat Stomach (treated with P1) S4= 7th Day Ulcer Rat Stomach (treated with Misoprostol);

c) Estimation of EGF-R and Smad-4 by RT-PCR:

The expressions of genes were studied through PCR analysis. After the experiment DNA bands were obtained through Agarose gel electrophoresis. The result was documented by Gel Documentation instrument. The bands showed that P1 treated gastric tissue expressed EGF-R and Smad-4 gene. Misoprostol expressed EGF-R to a lesser content. On the onset of ulcer (U0) Smad-4 showed a faint band.

6. Estimation of SMAD-4 by Immunohistochemistry:

SMAD-4 protein is a component of the TGF-□ pathway, which is known to increase the healing of gastric ulcer or any other tissue damage. The TGF□ pathway in turn is related with the EGF regulation pathway, so activation of SMAD-4 refers to the activation of EGF regulation pathway also.



S1= Normal Rat Stomach S2= 0th Day Ulcer Rat Stomach S3= 7th Day Ulcer Rat Stomach(without treatment) S4= 7th Day Ulcer Rat Stomach (treated with P1); S5=7th Day Ulcer Rat Stomach (treated with Misoprostol)

Smad-4 level was decreased in the ulcer 0th day ulcer tissue, which increased in the 7th day ulcer tissue. But the treated groups showed a good increase in the smad-4 expression. P1 proved to be the most effective in increasing the expression of Smad-4, whereas, the Misoprostol and E4 also showed a significant increase.

Discussion:

Ethanolic extract of leaves of Piper betle was shown from the similar laboratory to exhibit significant healing effect on the NSAID-induced gastric ulcer as evident from various biochemical parameters.(ref.). It was also shown in our previous paper that Ulcer formation , induced by Indomethacin, an NSAID, is related to the inhibition of the cyclooxygenase, that prevents the prostaglandin biosynthesis and in turn inhibits the release of the defensive factors of the stomach, mucin. The ulcer index showed that PBE gives 78.28% protection if 0th day ulcer is taken as 100% ulcer. Whereas,P1 gives 93.41% protection; and synthetic drug gives 85.39% protection.

Results show that treatment with the extracts significantly decrease the level of lipid peroxidation product, TBARS in gastric

tissue compared to ulcerated rats (fig 17 and table6). The decrease in the peroxidation level of lipid indicates a plausible mechanism of free radical involvement. The peroxidised lipids are the products of ROS damage on the cell membrane leading to disintegration and de-structuring of the fluid dynamic mosaic model, leading to cell death and formation of ulcer.

NSAIDs are known to induce ulcers during the course of their anti-inflammatory action by prostaglandin synthatase inhibition (through cyclooxygenase pathway). Immunohistological data showed that COX-1 and COX-2 comes to a level after a depression in cox-1 and slight increase in cox-2 level by the induction of NSAID, in the ulcerated model. On the 7th day both the COX-1 and 2 level increases. But with the extracts the cox-1 level rises much than the rise in COX-2.Recently it has been found that various gastric stressors (NSAIDs, alcohol, oxidative stressors, and acids) decrease the number of viable gastric pit cells by inducing both apoptosis and necrosis.(295,296) Thus, increasing the number of gastric pit cells could provide a new target for anti-ulcer drugs. In fact, growth factors for gastric mucosa were shown to be effective in combating ulcers in rats by increasing the number of gastric pit cells present (297). Hence activation of SMAD group of proteins could provide the basis of new types of anti-ulcer drugs, which increase the number of gastric pit cells by inhibiting their spontaneous apoptosis and stimulating their cell proliferation.

PCR is the best method to see the expression of certain genes in any tissue. In our experiment, EGF and SMAD protein were over- expressed in the P1 tissue, which is a direct proof of their up-regulation during the healing by these components. The present investigation thus emphasizes on the basic and fundamental research, detailing the effect of P1 in eradicating gastric ulcer. The plausible mechanism of P1behind the healing activity can be many, including their antioxidant property, immunomodulatory property, growth factor promoting property as well as COX up-regulating property. Our study explores the possibility for the development of some new drugs from plant source that become all the more relevant for an economically weak country, like India, which is rich in natural resources. The study is based on the fact that the ethanolic extracts of Piper betle leaves accelerate the healing of gastric ulcer induced by Indomethacin. The importance of the present study multiplies as the active components of it, which is a simple molecule like allylpyrocatechol, is proved to be a very good agent in healing gastric ulcer.

References:

1. **Hawkins C,Hanks GW.** The gastroduodenal toxicity of nonsteroidal anti –inflammatory drugs:a review of the literature.J Pain Symptom Manage 2000;20:140-151

2. **Pace V.** Use of Nonsteroidal anti inflammatory drugs in cancer.Palliat Med 1995; 9:273-286

3. Coruzzi G,Menozzi A,Dobrilla G. Novel non –steroidal anti-inflammatory drugs:what we have learned from animal studies.Curr Drug Targets Inflamm Allergy 2004;3:43-61.

4. 4. Garner A. Adaptation in the pharmaceutical industry with particular reference to gastrointestinal drugs and disease. Scan J Gastroenterol Suppl 1992; 193:83-89

5. 5. Dhikav V, Sing S,Pande S, Chawla A,Anand KS. Nonsteroidal drug-induced gastrointestinal toxicity: Mechanisms and Management Indian Clin Med 2003:4;315-322

6. 6. MiedererSE. Will anti–cancer drugs soon differ only in their side effects? Fortschr Med

1986;104:918-920

7. 7. Borrelli F, Izzo AA. The plant kingdom as a source of antiulcer remedies. Phytother Res 2000;14:581-591

8. 8. Yesilada E, Gurbuz I. A compilation of the studies on the antiulcerogenic effects of medicinal plants, Vol II: Phytochemistry and pharmacology .Singh S, Singh VK, Govil JN, editors. Hounton SCI Tech Publishing LLC.2003:111-174

9. Chatterjee A,Pakrashi SC. Treatise of Indian Medicinal Plants.New Delhi.CSIR Publication ,1995;26

10. Prabhu MS, Platel K, Saraswathi G, Srinivasan K. Effect of orally administered betel leaf (Piper betle Linn) on digestive enzymes of pancreas and intestinal mucosa and on the bile production in rats.Indian J Exp Biol 1995;33:752-756

11. Majumdar B, Ray Chaudhury SG, Ray A, Bandyopadhyay SK. Effect of ethanol extract of leaf of Piper betle Linn on healing of NSAID –induced experimental ulcer –A novel role of free radical scavenging action. Indian J Exp Biol 2003:41:311-315

12. Rathee JS, Patro BS, Mula S, Gamre S, Chattopadhyay S. Antioxidant activity of Piper betle leaf extract and its constituents. J Agric Food Chem 2006; 54:9046-9054

13. Szabo S, Trier JS, Brown A, Schnoor J, Human HD, Bradford JC. A quantitative method for assessing the extent of experimental gastric erosions and ulcers. J Pharmacol Methods 1985;13:59-66

14. **Esterbauer H, Cheeseman KH .** Determination of aldehydic lipid peroxidation products : malonaldehyde and 4-hydroxynonenal.Methods Enzymol 1990; 186:407-421

15. Palamanda JR, Keherer JP. Inhibition of protein carbonyl formation and lipid peroxidation by glutathione in rat liver microsomes.Arch Biochem Biophys 1992; 293:103-109.

16. Burton K. A study of the conditions and mechanism of the diphenylamine reaction for the colorimetric estimation of deoxyribonucleic acid .Biochem J 1956; 62, 315-323

17. Luck H . Catalase. In :Methods of Enzymatic Analysis Bergmeyer HU , Editor , New York:Verlay Chemical and Academic Press.1963:885-888

18. McCord JM, Fridovich I. Superoxide dismutase.An enzymatic function for erythrocuprein (Hemocuprein). J Biol Chem 1969, 244:6049-6055

19. Corne SJ, Morrissey SM, Woods RJ. Proceedings :A method for the quantitative estimation of gastric barrier mucus.J Physiol 1974:242:116P-117P

20. Winzler RJ. Determination of serum glycoproteins. Methods Biochem Anal 1955 ;2:279-311

21. Chang FY, Chen TS, Lee SD, Doong ML, Wang PS. Misoprostol –inhibited rat gastric emptying is independent of gastric inhibitory polypeptide release.Pharmacology 1999;58,265-269

22. Biswas K, Bandyopadhyay U, Chattopadhyay I, Varadaraj A, Ali E, Banerjee RK. A novel antioxidant and antiapoptopic role of omeprazole to block gastric ulcer through scavenging of hydroxyl radical. J Biol Chem 2003;278:10993-11001

23. McAlidon ME, Muller AF, Fillipowicz B, Hawkey CJ. Effect of allopurinol, sulphasalazine, a vitamin C on aspirin induced gastro-duodenal injury in human volunteers.Gut 1996; 38:518-524

24. Santos FA, Rao VS. 1,8-cineol, a food flavoring agent , prevents ethanol –induced gastric injury in rats.Dig Dis Sci 2001; 46:331-337

25. Bilici D, Suleyman H, Banoglu ZN A, Avel B, Ciftcioglu A, Billci S. Melatonin prevents ethanol – induced gastric mucosal damage possibly due to its antioxidant effect.Dig Dis Sci 2002 : 47:856-861

26. Bhattacharya S, Subramanian M, Roychaudhury S, Bauri AK, Kamal JP, Chattopadhyay S, Bandyopadhyay SK. Radioprotective property of ethanol extract of piper betel leaf. J Radiol Res (Tokyo) 2005: 46:165-171

27. Marotta F, Tajiri H, Safran P,Fesce E, Ideo G. Ethanol related gastric mucosal damage: evidence of a free radical mediated meachanism and beneficial effect of oral supplementation with bio-normalizer, a novel natural antioxidant. Digestion 1999;60:538-543

28. El-Missiry MA, EI-Sayed IH, Othman AI.

Protection by metal complexexwith SOD- mimetic activity against oxidative gastric injury induced by indomethacin and ethanol in rats.Ann Clin Biochem 2001; 38:694-700

29. Szabo S, Hollander D. Pathways of gastrointestinal protection and repair :mechanism of action of sucralfate.Am J Med 1989; 86;23-31

30. Tabor CW, Tabor H. Polyamines. Annual Rev Biochem 1984; 53: 749-790

31. Wang JY, Hsieh JS, Huang TJ. Changes in rat gastric mucosal glycoproteins in portal hypertension.Eur Surg Res 1997;29:280-286

32. Rainsford KD. The effects of aspirin and other non-steroid anti–inflammatory /analgesic drugs on gastro-intestinal mucus glycoprotein biosynthesis in vivo: relationship to ulcerogenic actions. Biochem Pharmacol 1978;27:877-885

33. Naito Y, Yoshikawa T, Matsuyar K, Yagi N, Arai M, Nakamura Y, Nishimura S, Yoshida N, Kondo M. Effects of oxygen radical scavengers on the quality of gastric ulcer healing in rats.J Clin Gstroenterol 1995;21 Suppl 1:S82-S86

34. James AH . Gastric epithelium in the duodenum . Gut 1964; 5:285-294

35. Chang CC, Pan S, Lien GS, Liao CH, Cheng YS. Deformity of duodenal bulb, gastric metaplasia of duodenal regenerating mucosa and recurrence of duodenal ulcer :a correlated study.World J Gastroenterology 2005 ;11:1802-1805

36. Alanko J, Riutta A , Holm P, Mucha I, Vapaatalo H, Metsa Ketela T. Modulation of Arachidonic acid metabolism by phenopls;relation to their structure and antioxidant /prooxidant properties .Free Radic Biol Med 1999; 26:193-201

Abbreviaion Used:

APC: Allyl pyrocatechol (P1) ; COX: Cyclooxygenase; EGF: Epidermal Growth Factor; EGF-R: Epidermal Growth Factor-Receptor; MDA: Malondialdehyde; PBE: Piper betle; Linn Ethanolic extract; TBARS: Thio-barbituric acid reactive substances

Correspondence Address: **Biswajit Majumdar**, Associate Professor of Biochemistry, Nobel Medical College , Biratnagar, Nepal. Mobile : +977 9814333690/ +91 9007753048, E Mail :biswajitmajumdar2005@yahoo.ca; biswajitmajumdar_78@hotmail.com

A PROSPECTIVE STUDY OF THE MANAGEMENT OF OPEN FRACTURES OF TIBIA

Abul Kalam Mohammad, Mahesh Shrivastav, Pradeep Gupta, and Awais Sayed

Abstract:

A Prospective study of 30 cases of type III open fractures of tibia is conducted at Nepal Medical College, Kathmandu and Nobel Medical College, Biratnagar from 2009 to 2011. All cases included in the study were initially managed by wound debridement and external fixation, and followed-up regularly for 10 months for outcome. Five cases developed deep infection and 10 had superficial infection, which subsided with prolonged use of antibiotics. Union was obtained in 7to 8 months for 28 cases. Two cases resulted in non- union which had been managed by bone grafting. Open Type III fractures of tibia are still a difficult and challenging problem for orthopedic surgeons. Almost all cases are required for twice surgery including secondary closure, skin grafting and readjustment.

Key words: *Open tibial fractures, External fixator.*

Introduction:

Open Type III fractures of tibia are very common due to road traffic accidents. It can be life threatening injuries and can cause severe permanent disability. Decision making on preferred treatment is complicated due to higher energy injury. External fixation is accepted by most orthopedic surgeons as the treatment of choice for Type III open tibial fractures because of its easiness for prolonged period of dressing, early stabilization and reconstruction of soft tissue envelop[1,2,3.]

Material and methods:

A prospective study of all consecutive patients over the period of study, 2009-2011, fulfilling the inclusion criteria were enrolled in the study. Those who were below 12 years of age and were suffering from diabetes mellitus were excluded from the study. Similarly cases who did not give the consent and were unable to complete their follow-up were also excluded from the study.

All subjects enrolled in the study were treated under C-arm mobile image intensifier by early and proper wound toilet and the application of AO type external fixator and were maintained on IV antibiotics, regular dressing and early mobilization. Patients were mobilized as soon after adequate soft tissue healing. The patients were non-weight bearing until the adequate bone union. Bone grafting was done within first four months. The duration of external fixator was determined by the operative surgeons, based on the state of the soft tissues and the extent of bone union. Sometimes the patients desire to have the fixator removed.

Results:

A total number of 40 patients with type III open tibial fractures were initially enrolled in the study. They were treated with external skeletal fixation. Out of 40 cases initially enrolled, 06 cases absconded and did not appear in their follow-up visits; similarly 04 cases were also referred to plastic surgeon for management of skin problems.

Out of 30 cases, who completed the study, 10 of the cases were male (33.33%) and 20 were female (66.66%), with mean age near about 30.5 years.

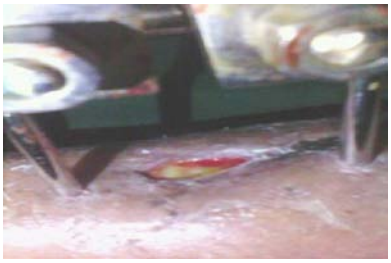
There were 16 Type III A fractures with an average time to union of 28 weeks. The average period of external fixation was 14 weeks (12-16 weeks).The average hospitalization time was about two weeks and to work was at an average of 36 weeks after the fracture.

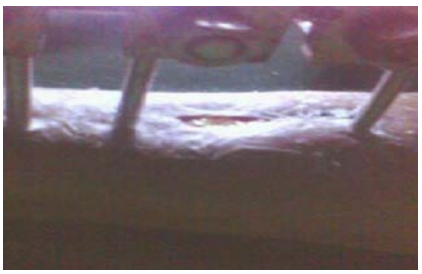
There were 12 Type III B fractures with an average time to union of 32 weeks. Of these 4 patients had extensive osteomyelitis and 6 had superficial wound. 2 patients who had extensive wound infection had to undergo secondary procedures like bone grafting and skin care. 6 patients had pin track infection and losing of pins and in these patients the external fixator was readjusted. Two (16.6%) patients developed nonunion and were readmitted for other procedures. Of the fractures that united 10 had an acceptable position giving over all valgus rates of 20%.

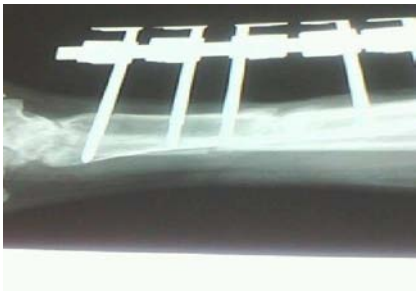
The average hospitalization time was one month. Most of the patients returned to work after 14-15 month of surgery.

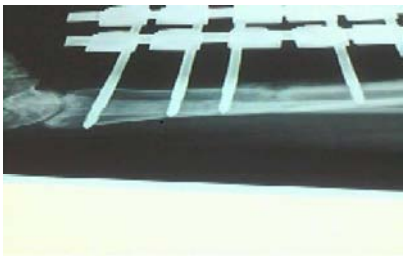
There were 2 Type III C fractures with an average time of union about 40 weeks. Both of them undergone multiple surgical procedures.

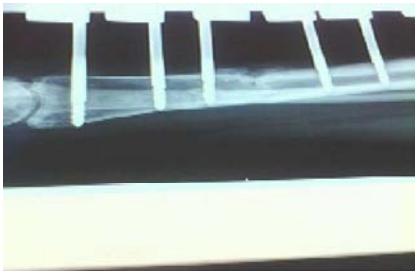
In our study some of the patients had fixator removed at an early stage because of psychiatric problems and was placed in a patellar tendon bearing cast until union had completed











Discussion:

Our results is in consistent with some of other studies that used external fixation in Type III open fractures[4,5,6.] We found excellent result for open tibial fractures treated with external fixator system. Orthopaedic surgeon treating open fractures of tibia by external fixator system because of strong gripping of fracture sites. So this system controls the movement and rotation of fracture sites as well as very easy for proper dressing. A previous reviewed had shown the poor results if the fixator were removed earlier[7,8.]

In our study mean time of union is 33.3 weeks. Chan et al (1984) reported 41% incidence of malunion and 62% incidence of joint stiffness.[4] The results for the different fractures subtypes highlight the importance of classifying these fractures adequately and suggest that the criteria on which Gustile et al based there sub-classification of type III fractures are appropriate[9.]

It is clear that each of the type III subtypes carries a very different prognosis. Type III A fractures are associated with a low incidence of infection and a relatively excellent functional result, with earlier return to Type III B fractures carry a significantly not so good prognosis, not only in the time to union but in the marked increased in the incidence of osteomyelitis. The hospitalization time for type III B fractures in our series averaged 40 days. Return to work was delayed. Prognoses for type IIIC fractures are poor.

Generally open type III fractures which were not reduced properly at the time of initial reduction but in our study image intensifier used and try to fracture sites reduced almost in proper position. Good results depend on good surgical technique and early skin cover. We found excellent result for open tibial fractures treated with external fixator system. Orthopaedic surgeon treating open fractures of tibia by external fixator system because of strong gripping of fracture sites[10,11.] So this system controls the movement and rotation of fracture sites as well as very easy for proper dressing

Conclusion:

External Fixation Systems of open type III fractures of tibia is a gold standard method of treatment with advantages of low rate of wound infection and early mobilization.

References:

1. **Behrens F, and Searls K**. External fixation of tibia: basic concept and prospective Valuation. J.B.J.S:1986; 68 B: 264-54.

2. **Burgess et al**. Management of type III open tibial fractures. orthop clin am 1987 ; 18:85-93.

3. **Caudle Rj, and Stern** PJ. Open fractures of tibia J.B.J.S:1987; 69-S:801-7

4. **Chan et al**. Management of type III open tibial fractures. Injury, 194; 16:157-65.

5. **Chapman M.W**. Role of intramedullary fixation in open fractures. Clin orthrop 1986; 212:26-34.

6. **Court et al**. External fixator in management

7. **Gustilo RB and Anderson JT**. Prevention of infection in long bone fractures. J.B.J.S, 1976; 58-A: 453-8.

of tibial fractures. JR soc Med 1985; 78:830-7

8. **Karlstorm G, Olerud**. External fixator in ioen tibial fractures.J.B.J.S.1980; 62-A:1264-73

9. **Lange et al**. Open tibial fractures with associated vascular injuries: Prognosis for limb salvage .J. Trauma 1985;25:203-8

10. **Lawyer et al**. External fixation in open tibial fracture J.B.J.S 1980; 62-A: 1264-73.

11. **Velazco A, and Fleming LL**. Open tibial fractures treated by external fixation. Clin Orthop 1983;180:125-32

Correspondence Address: **Dr. Abul Kalam Mohammad**, Department of Orthopedics, Nobel Medical College and Teaching Hospital, Kanchanbari-5, Bitatnagar.

AWARENESS OF DISEASE AND SELF CARE AMONG HYPERTENSIVE PATIENTS ATTENDING TRIBHUVAN UNIVERSITY TEACHING HOSPITAL, KATHMANDU, NEPAL.

Buna Bhandari, Mahesh Bhattarai, Manjul Bhandari,and Nilambar Jha

Abstract:

Background: *Hypertension (HTN) is a major risk factor for cardiovascular and renal diseases. The prevalence of hypertension has substantially increased during the past four decades. Information on prevalence as well as awareness regarding treatment and prevention of hypertension is scarce particularly in rural settings. The levels of awareness, treatment, and control of HTN vary between different countries and population groups*. Objectives: The objective of this study was to find out the awareness of hypertensive patients about *their own disease and self care.* Methodology: *Descriptive cross sectional study was conducted among 50 hypertensive patients who were admitted to Tribhuvan University Teaching Hospital (TUTH) and attended to medical OPD. Data was collected by using interview schedule by face to face interview method.* Results*: Among 50 hypertensive patients, 56% were aware about meaning of hypertension, 68% symptoms, 34% cause, 62% prognosis, and 62% complication of HTN. Likewise regarding self care, 70% were doing regular follow up, 92% using regular medication, most of them (80%) were not smoker and 84% were non alcoholic, and 74% taking low fat and low salt diet.* Conclusion: *Study finding reflects many of them (56%) had more than 50% of knowledge about the hypertension and more than half (54%) were giving more than 50% emphasis about their own self care.*

Key words*: Awareness, Hypertension, Control, Self care, Treatment*

Introduction:

Hypertension (HTN) affected 26.4% of the world's adult population (972 million) in 2000, and the rates are expected to increase to 29.2% (1.56 billion) by 2025. In particular, the global burden of HTN is highest in developing countries, although the prevalence may be comparatively lower than that in developed countries.[1] Cardiovascular disease is rapidly becoming a major cause of morbidity and mortality in developing countries throughout the world.[2,3] Hypertension is one of the major risk factors leading to an increased risk of stroke, myocardial infarction, end-stage renal disease, congestive heart failure and peripheral vascular disease.[4] Despite the availability of effective agents, the control rate is low, with less than 5% of patients with hypertension having adequate control[5.] HTN can be effectively controlled by antihypertensive drug therapy, educational and lifestyle interventions.[6,7] Unfortunately, the levels of awareness, treatment, and control of HTN vary between different countries and population groups. HTN awareness among hypertensive individuals ranged from 25.2% to 75.0%, whereas treatment ranged from 37.9% to 89.6% among

those aware of their HTN status.[8]However, little is known about the factors associated with awareness, treatment and control of HTN. Therefore, information on prevalence, awareness, treatment, and control and self care of hypertension in these poor resource settings is very scarce. The aim of the present study is to further elucidate the demographic factors that are associated with the awareness about disease and self care in order to better understand public awareness of the problem. This information is a pre-requisite to improvement of current clinical management.

Methodology:

Descriptive cross sectional study was conducted in the Medical Ward and Medical OPD of Tribhuvan University Teaching Hospital, Maharajgunj Kathmandu among the known cases of hypertension. A total of fifty hypertensive patients were included in the study following non probability purposive sampling method and adult patients with hypertension were included in the study whereas those who had developed complication of hypertension and severely ill patients were excluded from the study. Semi structured and structured interview schedule was used to collect necessary information using face to face interview technique by the researcher herself. For calculation of knowledge score, total nine questions regarding knowledge of hypertension and sixteen questions regarding self care was asked to all patients. Each affirmative answer was given one mark and total percentage was calculated based on their answers. Validity and reliability of the instrument was maintained by doing extensive literature review, consulting with experts and doing pretesting of the questionnaire. Collected data was checked, rechecked and edited at the end of data collection and coding and categorization was done. Data entry and analysis was done using Microsoft Excel and SPSS 11.5 version. Verbal consent was taken from the participants to participate in the study. Respondents were acknowledged for their participation in the study.

Results:

Among 50 hypertensive patient, many (44%) of the respondents were among middle age group. Higher percentage were male (54%) and (52%) from rural area. More than half (64%) were literate and 46% were suffering from hypertension between 1 to 5 yrs**. (Table no. 1)**

The awareness of hypertensive patient about their own disease is shown in **Table 2**, More than half (56%) of them were aware about the meaning of hypertension and 58% thought that the most common age group susceptible for hypertension is middle age group (40 to 59yrs). Regarding the reason of hypertension 34% thought that it is due to hereditary and stress. Another 34% thought that it is due to all the reasons like age, obesity, smoking, alcoholism, stress and hereditary factors. Most of them (84%) were aware about sign and symptoms of hypertension. Regarding prognosis, 62% of them thought it is controllable whereas 4% had no knowledge about it. And almost all patients were aware about control measure of hypertension and 62% of them knew about complications of hypertension.

Table 1: Distribution of Socio demographic variables of respondents (N=50)

Characteristics	Categories	No	Percentage
Age in years	20 - 39	10	20
	40 – 59	22	44
	60 and above	18	36
Sex	Male	27	54
	Female	23	46
Residence	Rural	26	52
	Urban	24	48
Education Status	Literate	32	64
	Illiterate	18	36
Duration of hypertension	Less than 1 years	14	28
	1 – 5 years	23	46
	5- 10 years	4	8
	More than 10 years	9	18

Regarding the habit of doing self care related to their own disease, 80% were not smoker and almost 84% did not have habit of taking alcohol **(Table 3).** Most of them (74%) had habit of taking low salt and low fat diet. More than half (64%) had habit of doing regular physical exercise and 62% were using different measure to reduce stress. Similarly 92% of them were taking their medication regularly but some of them (10%) were changing their doses of their medication by themselves. Thirty percent of them were discontinuing their medicine anytime. It was very good practice that 70% of them were doing regular follow up, and 74% were checking their blood pressure regularly.

Maximum knowledge score about hypertension is 88.8% (8) was obtained by 10% (5) of respondents and minimum score was 22.2% (2) by 4% (2) respondents. Similarly the maximum score of awareness about self care was 87.5% (14) was obtained by 4% (2) of respondents and minimum score was 26.5% (4.25) which was obtained by 2% (4) of respondents

.

Table 2: Distribution of respondents according to their knowledge about hypertension (N=50)

Knowledge	Responses	No	percentage
Meaning of hypertension	Yes	28	56
	No	22	44
Beliefs of most affected age group	20- 39yrs	4	8
	40- 59yrs	29	58
	60 yrs and above	3	6
	No idea	14	28
Reason of hypertension*	Overweight and old age	11	22
	Smoking and alcoholism	13	26
	Hereditary and stress	17	34
	All of above	17	34
Sign and Symptoms of Hypertension*	Dizziness and fatigue	24	48
	Headache and palpitation	32	68
	Flushing face and blurred vision	13	26
	No idea	8	16
Prognosis	Controllable	31	62
	Curable	9	18
	Not curable	8	16
	No idea	2	4
Control Measures*	Reducing weight and stress	16	32
	Intake of low salt and low fat diet	43	86
	By regular exercise	23	46
	By medication	26	52
Complication of hypertension	Know	31	62
	Don't know	19	38

* = *Multiple response answers*

Table 3: Distribution of respondents about habit of doing self care (N=50)

Self care practices	**Responses**	**No**	**percentage**
Smoking	Yes	10	20
	No	40	80
Alcoholism	Yes	8	16
	No	42	84
Dietary habit	Low fat and salt diet	37	74
	Low salt	11	22
	Low fat	2	4
Physical Exercise	Regular exercise	32	64
	No regular exercise	18	36
Using Measure to reduce stress	Yes	31	62
	No	19	38
Taking medication	Regularly	46	92
	Irregularly	4	8
Changing dose by themselves	Yes	5	10
	No	45	90
Discontinuing medicine anytime	Yes	15	30
	No	35	70
Follow up	Regular	35	70
	Irregular	15	30
Monitoring blood pressure	Regularly	37	74
	Irregularly	13	26

Discussion:

Health care resources are scarce, and focusing investment in areas that would render the greatest benefits with the least cost needs to be identified. Morbidity and mortality from cardiovascular disease is high. Self-care can be defined as activities that a patient undertakes with the intention of improving health or preventing disease. Self-care for hypertension includes taking medicine as prescribed, monitoring blood pressure response to therapy, and adopting lifestyle recommendations increasing exercise, decreasing salt intake. Present study examined the level of awareness of hypertensive patients about their own disease and self care. The prevalence of hypertension was higher 44% among middle age groups (40-59yrs) followed by young adults (20-39yrs) 36% whereas WHO study 1996[9]showed 30% in above 30yrs and 14.19% among young adults. In a study in the productive age groups (30–49 years), 36.5% of the males were affected and 27.1% of the female affected.[10] Our study showed male more suffered from hypertension 54% supported by other study[11].

This study showed 56% of respondents were aware about hypertension which is higher than the study done in China 29.5%[12] and study done in Kathmandu valley 41.1%. Main reason of hypertension given by respondents were hereditary and stress 34% and another 34%

thought all the given factors i.e. overweight, old age, smoking, alcoholism, hereditary and stress. This study reflects control of hypertension can be done by taking low fat and low salt diet similar to the other studies which showed by doing regular exercise, changing healthy dietary habits. These healthy activities can control blood pressure of 25% of people and reduce by 77% by controlling weight and 35% by reduction of sodium in diet.[13] Another study showed 80% of the patients knew they should limit their salt intake, only one third always avoided salty foods.[14]Patients should be advised that excess salt ingestion will increase blood pressure. Salt restriction could make the difference between needing only 1 rather than 2 antihypertensive agents. Daily smokers were less likely to be aware of having HTN or being treated, whereas ex-smokers were more likely to be aware of their diagnosis. A possible explanation might be that some smokers quit smoking by themselves or followed by physicians' advice after detection of HTN.

Individuals who drank alcohol were also more likely to be untreated if they had HTN.[15]Similarly this study shows 80% had no habits of smoking and 84% were not taking alcohol. Additionally, 25% of the patients did not appreciate the risk of alcohol use and 36% believed they should drink a lot of fluids.[14]The Joint National Committee 7 (JNC 7) also recommends that male patients consume not more than 2 alcoholic drinks per day and female patients no more than 1 drink per day. Limiting alcohol consumption may decrease (Systolic Blood Pressure) by 2 to 4 mm Hg. The JNC 7 recommends that patients involve themselves in aerobic exercise for at least 30 minutes per day on most days of the week. For approximately every 20 pounds of weight lost, it is believed that patients may reduce their SBP by 5 to 20 mm Hg.[16]This study showed more than half (64%) had habits of doing regular exercise supported by other study which mention that exercise can help to reduce blood pressure and keep weight down. It is also a good stress reliever.[17]This study found out 92% of them were taking their medication regularly and more than 90% never change their drug by themselves 70% of them did not discontinue their medication.

Despite the availability of effective treatment, over half of the patients being treated for hypertension drop out of care entirely within a year of diagnosis and of those who remain under medical supervision only about 50% take at least 80% of their prescribed medications.[18]Similarly the present study showed that 70% of them were doing regular follow up, and 74% monitoring their blood pressure regularly and 40% were using blood pressure control measure if their blood pressure increases. So highest knowledge score about awareness of hypertension was 88.8% by 10% respondents and highest knowledge score of awareness of self care was 87.5% obtained by 4% respondents.

Conclusion:

The results of present study suggest that level of knowledge about disease and self care is good among the study population. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure states that self measurement of blood pressure may benefit patients by providing information on response to antihypertensive medication and improving adherence with therapy. The study also notes that the patient and clinician must agree on blood pressure goals. That patient motivation to adopt lifestyle changes and take prescribed medication improves when patients have positive experiences. Study suggests that there should be more research to find out new strategies to tackle these issues of awareness and self care about Hypertension.

References:

1. **Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J**. Global burden of hypertension: analysis of worldwide data. Lancet 2005; 365:217–223.
2. **Murray CJ, and Lopez AD**. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. Lancet 1997; 349:1498–1504.
3. Fuentes **R, Llmaniemi N, Laurikainen E, Tuomilehto J, Nissinen A**. Hypertension in developing economies: a review of population-based studies carried out from 1980 to 1998. J Hypertens 2000; 18:521–529.
4. **Steyn K, Gaziano TA, Bradshaw D, Laubscher R, Fourie J.** Hypertension in South African adults: results from the demographic and health survey, 1998. J Hypertens 2001; 19:1717–1725.
5. **PRC National Blood Pressure Survey Cooperative Group**. Hypertension Prevalence and the Status of People Awareness, Treatment, and Control in China: A national-wide survey in 1991. Chinese J Hypertens 1995; 3 (suppl):S14–S18.
6. **Machado M, Bajcar J, Guzzo GC, Einarson TR.** Sensitivity of patient outcomes to pharmacist interventions. Part II: Systematic review and meta-analysis in hypertension management. Ann pharmacotherapy, 2007; 41:1770–1781.
7. **Fahey T, Schroeder K, Ebrahim S**. Educational and organizational interventions used to improve the management of hypertension in primary care: a systematic review. Br J Gen Pract 2005; 55:875–882.
8. **Kearney PM, Whelton M, Reynolds K, Whelton PK, He J**. Worldwide prevalence of hypertension: a systematic review. J Hypertens 2004; 22:11–19.
9. **The WHO report** " Hypertension Control",1996 pp 30-33
10. **Prasanth TS, Vijayakumar K**. Prevalence of Systemic Hypertension among the rural residents of Kerala. Calicut Medical Journal 2008; 6(3):e4.
11. **Badhu BP,shresthaJK**. Hypertension patient in eye OPD, TUTH. Journal of the IOM.1998; pp 188-192
12. **Guang-Hui Dong†, Zhao-Qing Sun**. Prevalence, awareness, treatment & control of hypertension in rural Liaoning province, China. Indian J Med Res 128, August 2008, pp 122-127
13. **Onta M**. Hypertension: AS tricking time bomb"Journal of Nursing "vol 1;1998:pp16-18
14. **Hanyu Ni, Deirdre Nauman, Donna Burgess, Kendra Wise; Kathy Crispell, Ray E. Hershberger**. Factors Influencing Knowledge of and Adherence to Self-care among Patients With Heart Failure. Arch Intern Med. 1999;159:1613-1619.
15. **Yi Wua, E. Shyong Tai et.al.** Risk factors associated with hypertension awareness, treatment, and control in a multi-ethnic Asian population. Journal of Hypertension 2009, 27:190–197
16. **Joint National Committee**, the 7th report of the joint national Committee on detection, Evaluation and treatment of high bold pressure. Archives of internal Medicine 1993,153:154-18
17. **T Diane**. Leaflet: Hypertension - self help measures. Steyning Health Centre; October : 2003
18. **Sackett DL**. Randomized clinical trial of strategies for improving medication compliance in primary hypertension. Lancet, 1975; 1:1205–1207.

Correspondance address: **Buna Bhandari Bhattarai**, Lecturer, Department of Community MedicineNobel Medical College and Teaching Hospital, Biratnagar, Nepal. E-mail: bhbuna@gmail.com, Cell. Phone: 9842037499

INCIDENCE OF ANEMIA BASED ON HAEMOGLOBIN LEVELS IN CHILDREN 2-12 YEARS OF AGED IN NOBEL MEDICAL COLLEGE TEACHING HOSPITAL, BIRATNAGAR, NEPAL

Amar Kumar Sinha And Biswajit Majumdar

Abstract:

Haemoglobin levels were used to estimate the incidence of anaemia in children 2-12 years old in the population of Biratnagar,Morang Dist., Nepal. who were attending Nobel Medical College & teaching hospital. Out of 5063 subjects, 634 children's were selectively diagnosed as anaemia. Among the 2406 children's aged 2-6 years 5.4% were diagnosed with mild anaemia,2.7% moderate anaemia and 1.7% severe anaemia (WHO definition) of 2657 children's aged 7-12 years,10.2% were diagnosed with mild anaemia, 3.1% moderate anaemia and 1.3% severe anaemia.

Kew Words: Incidence, Prevalence, Anaemia

Introduction:

Anaemia is the commonest problem in the growing age group in developing countries[1]. When iron deficiency is sufficient severe, Hb concentration in the blood decreases, leading to iron deficiency anaemia (IDA), which has negative health consequences, especially in children[3], adolescents[4].

According to the latest data more than 3 billion people throughout the world have some form of anaemia ranging from deficiency in iron resources without symptoms of anaemia to iron deficiency anaemia.[5] Iron deficiency in infancy and adolescence causes mental retardation and damages the immune system, predisposing children to a wide range of disorder.[6,7] Different studies in Egypt[8], India[9], Thailand[10] and the United states[11] have shown that iron-deficiency anaemia in children under 5 years old and primary school students is accompanied by psychomotor retardation, low intelligence and decreased learning capability. A study in Thailand has shown that the effects of anaemia on intelligence couldn't be compensated for[10] one of the most dangerous consequences is the higher risk of poisoning with heavy elements, since the absorption of these elements increases in cases of iron deficiency.[12] Recently it has been reported that preschool children have the highest prevalence of anaemia, nearly 50% across developing countries, compared with pregnant and non- pregnant women.[13]

Method and methodology:

This retrospective study was conducted in Nobel Medical College & Teaching Hospital (NMCTH) with aim to serve Nepalese people. A sample size of 5063 subjects who were investigated for estimation Hb levels by Cyanmethaemoglobin method both aged 2-6 years and 7-12 years children.As anaemia is classified into three degree according to WHO: mild, moderate and severe. Hb cut-off values of anaemia for children <6 years were mild 10.0-10.9 g/dl, moderate 9.0-9.9 g/dl and severe< 9.0 g/dl. Hb cut- off of anaemia for children 6-12 years old were: mild 11.0-11.9 g/dl, moderate 10.0-10.9 g/dl and severe < 10.0 g/dl[14]

Result:

Table:1: shows that 634 subjects were diagnosed as anaemia out of a total population of 5063 including both the aged 2-6 years and 7-12 years childrens in our study. The total percentage of anaemia was 24.4% comparatively among them, 241 and 393 were 2-6 years and 7-12 years children respectively. The incidence of anemia was 9.8% in 2-6 years and 14.6% in 7-12 years children. The overall incidence of anemia was significantly higher 14.6% aged 7-12 years of children.

Table:2 reperesents the status of anaemia based on Hb levels measured in 2-6 years old children, severe anaemia was seen in 1.7%, moderate anaemia was present in 2.7% and mild anemia was present in 5.4% of children . Overall incidence of anemia was 9.8%.

Table 1: Incidence of anemia in both 2-6 and 7-12 years children

Total No of Investigated Patients	Total Anaemic Patients	% of Anaemic Patients
5063	634	24.4%

Table 2: Distribution of anaemia based on the Hb levels in children aged 2-6 years and 7-12 years of Nobel Medical College and teaching hospital, Biratnagar, Morang district of Nepal

Age group/ severity of anemia	No of patients	%	Total %	
	*2-6 years			
	Severe Moderate Mild Total	43 66 132 2406	1.7 2.7 5.4 100.0	9.8
**6-12 years				
Severe Moderate Mild Total	36 84 273 2657	1.3 3.1 10.2 100.0	14.6	

Table: 2 also depicts the status of anemia based on haemoglobin(Hb) levels,in children 7-12 years old. Severe anemia was seen in 1.3%, moderate anemia was present in 3.1%, and mild anemia was present in 10.2% of children .The overall incidence of anaemia 14.6% .So it is significantly higher than the 2-6 years of children

***Discussion**:*

Our retrospective study one of the hospital based study. The study shows that anaemia should be considered as a major health problem in Biratnagar, dist., Morang, Nepal.

In total 9.8% of 2-6 year old children and 14.6% of 7-12 year-old children suffered from anaemia (Hbs 11.0 g/dl). According to the WHO classification if 5%-25% of the population have anaemia or abnormal Hb , the degree of population anaemia is graded

mild.[7]

A study in the United states (US) in 1976-80 showed the rate of anaemia to be around 6% in 2-6 year-old children.[15] Anaemia is present in 27% of 1-6 year- old children in the Philippines, 27%-44% in 3-5 year- old children in India and 24% in 2-5 year- old children in Romania.[16] Another report showed that Asian children suffer from micronutrient deficiencies, especially iron deficiency anaemia and the prevalence of iodine- deficiency anaemia was 40-50% in preschool and primary- school children.[17]

The world Health organization has proposed that if the prevalence of anaemia in a region is between 5% and 20%, appropriate interventions based on food diversification, food fortification, iron supplementation and controlling infectious diseases should be considered.[7] Weekly iron supplementation for school children considered for primary schools. Fortification of foods (Such as iron fortification of biscuits) is another strategy which could be considered for preventing iron deficiency among Nepalese school children.

References:

1. **De Maeyer E, Adiels-Tegman M**. The prevalence of anaemia in the world. World Health Stat Q. 1985 38,302-316.

2**. WHO U** (1998). World Health Organization, UNICEF & UNU Iron Deficiency.Indicators for Assessment and Strategies for prevention 1998.

5. **Michaelson KF et al, eds**. Feeding And nutrition of infants and young children. Copenhagen, World Health Organization Regional Office for Europe, 2000,WHO European Series. N0. 87

6. **Scrimashaw NS**. Functional significance of iron deficiency: an overview. In: Enwonwu CO, ed. Functional significance of iron deficiency. Annual nutrition workshop series, Volume lll. Nashville,Tennessee,Meharry Medical College, 1990:1-13.

7. Iron deficiency anaemia. Assessment, prevention and control. A guide for programme managers. Geneva, World Health Organization, 2001, WHO/NHD/01.3

8. **Seshadri S, Gopaldas T**. Impact of Iron supplementation on cognitive functions in preschool and school aged children: the Indian experience. American journal of clinical nutrition, 1989, 50:675S-84S.

9**. Soemantri AG**. Preliminary finding on iron supplementation and Learning achievements of rural Indoesians childrens. American journal of clinical nutrition, 1989, 50:687S-96S.

10**. Pollitt E et al**. Iron deficiency and educational achievement in Thailand. American journal of clinical nutrition, 1989, 50:687S-96S.

11**. Pollitt E**. Effects of a diet deficient in iron on the growth and development of preschool and school aged children. Food and nutrition bulletin, 1991, 13:110-18

12. **Masawe MJ**. The adverse effect of iron retention on the course of certain infections. British medical journal, 1987 , 2:1113-15.

13**. Mason J et al**. Recent trends in developing regions: vitamin A, anemia iodine deficiency and child underweight. Food and nutrition bulletin, 2005, 26(1):59-108.

14. **Mohammed K, Malekafzali H.** Nationl Health and Diseases Survey in the Islamic Republic of Iran. Tehran, Undersecretary for Reaserch, Ministry of Health and Medical Education, 1999.

15. **Dallman PR,Yp R, Johnson C**. Prevalence and causes of anemia in the United States, 1976 to 1980. American journal of clinical nutrition, 1984, 39:437-45.

16. **Nestel P,ed**. Proceeding: iron interventions for child survival. London, United States Agency for International development (USAID), Opportunities for Micronutrient Interventions (OMNI), and Institute for Child Health (ICH), 1995.

17**. Khor GL**. Update on the prevalence of malnutrition among children in Asia Nepal Medical College journal, 2003, 5(2):113-22.

Address for correspondence: **Amar Kumar Sinha**, Associate Professor, Department of Biochemistry, Nobel Medical College, Biratnagar, Morang., Nepal. E-mail: drak_sinha@yahoo.com

A STUDY ON PERSONAL HYGIENE AND SANITARY PRACTICES IN A RURAL VILLAGE OF MORNAG DISTRICT OF NEPAL

Rajiv Ranjan Karn, Buna Bhandari, and Nilambar Jha

Abstract:

Background: Inadequate sanitation has direct effect on health of individual, family, communities and nation as a whole. Objective: To assess the personal hygiene and sanitary condition of the Katahari Village Development Committee (VDC). Methods: The cross sectional study was done in Katahari VDC of Morang district. A total of 80 households were randomly selected from two wards of VDC. The data were collected by interview method using interview schedule. Data were entered in Excel sheet and analyzed on SPSS program. Results: Many respondents (61%) were unable to read and write, 33% involved in private job in various factory. Knowledge of sanitation was high (90%) but only 65% of them were using soap water for hand washing. Sixty percent had no toilet facilities. There was significant association between education and toilet facilities among community people. Land holding and type of family had no significant association with toilet facilities. Conclusion: The knowledge regarding sanitation was high among community people but very poor in practice.

Key words: Personal hygiene, Sanitation, Hand washing practices, Rural area, Nepal

Introduction:

Inadequate sanitation has direct effect on health of individual, family, communities and nation as a whole. Simply, having sanitation facilities increases health well-being and economic productivity. Sanitation includes use of latrine, personal hygiene, clean surrounding, proper disposal of solid and liquid wastages and hygienic behavior. Toilet is taken as an essential and basic indicator of health and sanitation worldwide[1]. Proper sanitation is a necessary prerequisite for improvement in general health standards, productivity of labour force and good quality of life[2]. Every 20 seconds, a child around the world dies as a result of poor sanitation[3]. About 80% of all disease of the developing world is related to unsafe water and inadequate sanitation[4]. Worldwide, 5.3% of all deaths and 6.8% of all disability are caused by poor sanitation, poor hygiene and unsafe water. Nearly two-thirds (67%) of the total population go for open-air defecation and only one-third (33%) having access to a latrine[5]. The lack of access to sanitation in Nepal is striking. A total of 75% of the population is without access to sanitation, one of the highest proportions in Asia. However, the urban sanitation coverage is 75% and the rural sanitation coverage is only 20%[6]. Every day, 16 million Nepalese (around 57% of the population) practice open defecation because they have no toilets[7]. Access to sanitary system, garbage disposal and toilets are lowest among the poorest population and is better in the richer quintiles of the population. There is huge gap in access to sanitary facilities between that available to the poorest population and the national average[8]. So this study aims to

find out the personal hygiene, sanitary condition of the Katahri VDC of Eastern Nepal.

Materials and Methods:

This cross sectional study was done in Katahari VDC of Morang District of Eastern Nepal which is situated near to Biratanagar. The study duration was of five month from Feb to June 2011. Two wards were selected randomly among the nine wards of VDC. Study population was 816 households. Among them sample size 80 households were selected purposively for data collection. The data was collected from every third house in each ward. The first house was selected randomly. For data collection, interview was conducted with the head of the household using a semi structured schedule. Observation was done using an observational checklist to assess the sanitary condition of latrines. Data was entered in excel sheet. Editing and coding was done and analyzed by using SPSS 15. The verbal consent was taken from the respondents before interview.

Results:

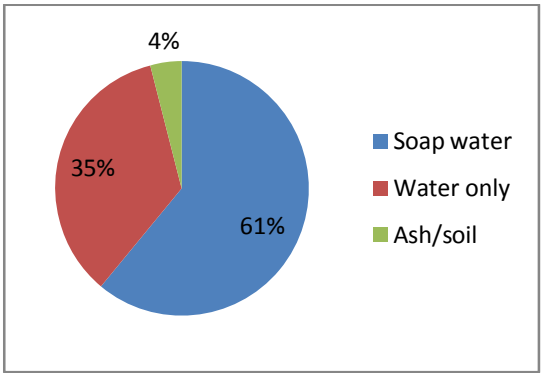
A total of 80 respondents were interviewed from 80 household in two wards (1 and 2) of Katahari VDC. Among them 72% were female and 28% were male. Most of them (82%) were Hindu and 18 % Muslim by religion. Most (61%) were unable to read and write and 32% were doing private job. Many (60%) had nuclear type of family. Sixty five percent had no land (Table-1).

Table 1. Socio-Demographic Characteristics of the Respondents

Socio-demographic Characteristics	Frequency (n=80)	Percentage
Sex		
Male	58	72
Female	22	28
Religion		
Hindu	66	82
Muslim	14	18
Education		
Unable to read and write	49	61
SLC and Above	31	39
Occupation		
Agriculture	11	14
Business	18	22
Government Job	11	14
Private Job	26	32
Labour	14	18
Type of Family		
Nuclear	48	60
Joint	32	40
Land		
Yes	28	35
No	52	65
Total	**80**	**100**

Most (65%) of the respondents used soap with water after defecation, 31% used water alone and 4% ash/soil with water for hand washing (Fig-1).

Fig. 1: Hand washing practice of the Respondents
Ss



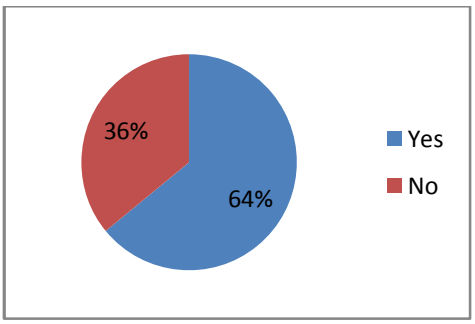
Most (90%) of the respondents had awareness regarding sanitation as they mentioned that due to lack of sanitation there is diarrhoeal and other kind of diseases. Ten percent didn't have knowledge about sanitation. More than half (58%) of the houses had satisfactory sanitary condition. Regarding personal hygiene 64% had good and 36% did not have good personal hygiene (Table 2).

Table 2. Knowledge of sanitation and personal hygiene among community people

Knowledge of sanitation	**Frequency**	**Percentage**
Knowledge	72	90
No knowledge	8	10
Sanitary condition		
Satisfactory	46	58
Un satisfactory	34	42
Personal Hygiene		
Yes	47	64
No	33	36
Total	**80**	**100**

The toilet facilities were seen only in 36% of houses (Fig 3).

Fig. 2: Toilet facilities in the communities



There was significant association between education and toilet facilities (P value<0.05) but there was no significant association between land and type of family among community people (Table 3)

Table 3. Association of toilet facilities with different variables

Variables	Toilet Facilities			
	Yes	**No**	**Total**	**P Value**
Education				
Unable to read and write	10	39	49	0.004
SLC and Above	16	15	31	
Land				
Yes	9	19	28	0.96
No	17	35	52	
Type of family				
Nuclear	13	19	32	0.207
Joint	13	35	48	
Total	**26**	**54**	**80**	

Discussion:

In this study most (65%) of the respondents were using soap water after defecation, and 31% were using water alone and 4% were using ash/soil water for hand washing. But the study done in Madhyapradesh India showed that 100% of people did not wash their hand after defecation they were using stone, soil and leaves for washing hand.[2] Similarly, the study done in Kathmandu,

showed that majority (36%) of the households had used soap with water after defecation[9]. As hand washing is directly concerned with personal hygiene, it is good practice that this community was using soap water 65% after defecation. In this study

64% had good personal hygiene practice and 36% did not had good personal hygiene and 58% of the houses had good sanitary condition. Similarly the study done in Madhyapradesh showed that environmental sanitation through inhabitants was of an average degree, but not very much satisfactory from the hygiene point of view[2]. The present study shows that 90% awareness about sanitation but the studies done in Bote community of Pragatinagar VDC of Nawalparasi district showed that only 15% of respondents were aware of hygiene. Most of them believe that ghosts spread of diseases[10]. In this study 64% of the houses didn't had toilet facilities and they use open defecation. According to Nepal MDG progress report, around 57% of the population of Nepal practice open defecation because they had no toilets. Similarly, the study done by Kravid DZ showed that only 5% of villagers used latrines[11]. In the study done by Thapa M showed that in most of the rural village, latrines are non-existent. The people used to discharge excreta near water sources, making water contaminated[12].

Conclusion:

The sanitary knowledge 90% and hand washing with soap water 65% of the community people was high. The toilet facility was low (36%). So, there should be extensive health education program for the people of the Katahari VDC about the personal hygiene and sanitation. Government and Non-governmental organization should be involved in the construction of toilet in this community with their full participation.

References:

1. **Environmental sanitation guidelines**, Rural Village Water Resources Management Project, 2009.

2. **Dwivedi P, Sharma A. N.** A Study on Environmental Sanitation, Sanitary Habits and Personal Hygiene among the Baigas of Samnapur Block of Dindori District, Madhya Pradesh, J. Hum. Ecol 2007;1:7-10.

3. **World Health Organization and United Nations Children's Fund** Joint Monitoring Programme on Water Supply and Sanitation and Water Supply and Sanitation Collaborative Council.

4. **Thapa M, Sharma AP**. Study of Bacteriological Treatment of Water for Rural Communities. Nepal Journal of Science and Technology. Royal Nepal; Academy of Science and Technology, Kathmandu 1999;1:27-33.

5. **Ahmed MF**. South Asian Conference on Sanitation, BCHIMES, (Between Census Household Information, Monitoring and Evaluation System; 2001.

6. **Patrick Webb.** Water and Food Insecurity in Developing Countries: Major Challenges for the 21st Century [online]. 2005 Oct 20 [cited 2007 Aug 5]; available from: URL:http://www.nutrition.tufts.edu/

7. **Nepal MDG Progress Report**. 2010, GoN and UNDP and CBS, 2009

8. **Winrock International, Nepal country environmental analysis**: Environmental sector review; revised draft prepared by World Bank [online] 2007 Feb 22 [cited 2007 Aug 7]; available from: URL:http://www.winrock.org.np

9. **Pradhan Bandana**. Rural communities knowledge on water quality and water borne disease: the case of Bungamati Locality in Kathmandu Valley, Nepal.

10. **Rosyara KP**. A study of the health and sanitary status of Bote community, an indigenous, Journal of Institute of Medicine. 2009

11. **Kravitz JD**. The effect of water supply, handling and usage on water quality in relation to health indices in a developing community in South Africa. Urban Health News. 1995; 26:32-6.

12. **Thapa M, Sharma AP**. Study of Bacteriological Treatment of Water for Rural Communities. Nepal Journal of Science and Technology. Royal Nepal; Academy of Science and Technology, Kathmandu 1999;1:27-33.

Address for Correspondence: ***Rajiv Ranjan Karn***, Lecturer, Department of Community Medicine, Nobel Medical College, Biratnagar. Email: rajiv2061@gmail.com Cell Phone: 9842068053

A STUDY OF SOCIO-DEMOGRAPHIC AND DIAGNOSTIC PROFILE OF PATINETS ATTENDENING THE PSYCHIATRIC OUT-PATIENT DEPARTMENT OF NOBEL MEDICAL COLLEGE, BIRATNAGAR

Naba Raj Koirala, Rajesh Yadav, Ajay Kumar Das, Jwalanta Poudel, and Santosh Kumar Bhagat

Abstract:

Study on prevalence of psychiatric disorders in Eastern part of Nepal, is relatively understudied subject in Nepal. The present study is undertaken with the aim to study the socio-demographic characteristics and diagnostic profile of patients attending the psychiatry OPD of Nobel Medical College, that provides both outpatient and inpatient services to psychiatric patients residing in eastern part of Nepal and nearby Indian villages. It was a retrospective study where all consecutive patients attending the Psychiatry OPD from 1st May 2011 to 30th April 2012 and fulfilling the diagnostic criteria for Category F of ICD-10[1] were included in the study. Amongst the total number of 637 patients, cases with Epilepsy (N=44), Headache (N=53), other medical disorders (N=13) and incomplete case record (N=17) were excluded, and the final sample size was comprised of 510 cases (males=214 and females=296). Maximum numbers of patients were in the age-group 16-40 years (N=238, 47%) and were married (N=416, 79.04%). Most of the patients suffered from Neurotic stress-related and somatoform disorders (N=214, 41.96%), followed by Mood (N=168, 32.94%) and Schizophrenia, schizotypal and related disorders (N=56, 10.98%).

Key words: OPD, Psychiatric Disorders, Nobel Medical College

Introduction:

The WHO estimate of people with mental disorders to be about 450 million (out of a total of 6 billion), with about 150 million suffering from depression, 25 million from schizophrenia, more than 90 million from alcohol or drug use disorders[2]. The impacts of this disorder are severe, with approximately 1 million people committing suicide annually. There is also an increase in co morbidity of this different conditions[2,3]. The mental disorders thus comprise a wide variety of disorders, some of which may not be acknowledged as ailment by many in the society, but still causing a lot of trouble to the sufferers and affecting the productivity of the persons and obviously of the nation. Moreover, the age group which is occupationally more active seems more affected by the disorders, many of which actually have good prognosis, suggesting the need for early identification and prompt management of these illnesses[3]. Awareness programs involving different cultural, occupational, and social groups of the society will definitely be fruitful. Mental disorders are mostly stigmatized in our communities and this affect the overall care of mental health care users.

Although attempts have been made by our many eminent psychiatrists in the past, the mental health professionals and policy makers

in the country still finds difficult to obtain reliable information regarding psychiatric morbidity in the country, both in the community and hospitals. Some of the noticeable studies conducted by K.C.& Shah, (1986)[4], Nepal et al (1986)[5] , Wright (1987)[6], Shrestha (1987)[7] and Sharma (1987)[8], show a similar findings in relation to age wise distribution but in many other aspects they are not conclusive and differ from each other, specially whenever the question of diagnosis is placed forward. All those inconsistencies may be because of the difference in methods and methodology used; the setup, subject enrolled in the study and diagnostic criteria used. Despite of all those inconsistencies their findings are always helpful for both the health care providers and policy makers to formulate a necessary policy and plan of action to encounter the difficulties and to improve the quality of mental health services in the country. Similarly many of available studies in mental health in Nepal mostly describes about the people living in the capital city of Nepal and nearby cities, and their findings may also not likely to be generalized. Therefore, keeping this point in mind, the present study is carried out in a city of Nepal; where from not a single study on epidemiology of mental health is reported in the literature until date. Hence this present study is carried out at psychiatric OPD of Nobel Medical College, Biratnagar, just as an attempt to enrich the available literature in the country in regards to socio-demographic characteristics and diagnostic profile of patients attending the psychiatry outpatient department of a tertiary level hospital in eastern part of Nepal.

Material and Method:

A retrospective study was designed with an aim to describe the socio-demographic characteristics and diagnostic profiles of patients attending the psychiatry outpatient department of Nobel Medical College over a period of one year, from 01 May 2011 to 30 April 2012. The objectives were set to study the age, sex, occupation and diagnostic profile of the patients attending the psychiatric out-patient department of the Nobel Medical College over the period of one year, so that the available information can be used in future to improve the quality of health mental health services that the institute has been delivering to the patients who have been deprived of it for quite long period of time. The subjects for this study were comprised by all those consecutive new patients attending the psychiatric out-patient department over the study period and fulfilling the diagnostic criteria for category F of International Classification of Diseases (ICD-10), 10th revision (WHO, 1992). All other cases with incomplete case records, other than ICD-10 Chapter F diagnoses, chronically debilitating patients, and follow-up cases were excluded from the study. The data required for the purposes of study was collected retrospectively using a self-designed proforma and stored in a personal computer and analyzed with help of SPSS version 11.

Results:

Table 1: Distribution of Patient according to age and sex

Age (Years)	Up to 16 Years	16-40 Years	40-60 Years	> 60 Years
Male	18	108	58	30
Female	34	130	91	41

Out of a total number of 637 new patients who attended the psychiatry OPD during the study period of 1 year, 44 cases of epilepsy, 53 cases with diagnosis of headache, 13 new cases with diagnosis of other medical disorder, and 17 cases with incomplete case record were excluded from the study. Thus the study sample for this study comprises of only 510 new patients fulfilling the diagnostic criteria

for mental and behavioural Disorder according to Category F of ICD-10, WHO 1992. Out of all those 510 new cases, enrolled further for study, 214 were male (42%) and 296 (58%) were female. Maximum patients were in the age group 16-40 years (N=238; 47%), followed by the age group 40-60 years (N=149; 29 %) (Table: 1).

Table: 2 Distribution of Patient according to Marital Status

Gender	Married	Single	Divorce	Separated
Male	131	78	2	3
Female	188	95	8	5

Majority of the patients were married (N=319; 62.5%), with significant high proportion for female (N=188; 36%) compared to male (N=131; 25%). (Table-2).

Table: 3 Distribution of Patient according occupation

Gender	Male	Female
Student	54	43
Govt. Employee	45	7
Private Employee	51	39
Idle	13	168
Semi Skilled/Labor	35	23
Self Employed	19	17

Table 3 shows that out of all 510 subjects enrolled in the study 97 (Male 54; 11%; Female 43; 8%) were students and only 49 were government employed. There were high preponderance of female (N=167; 33%) who were idle and engaged themselves at household activities. The result also shows that only few cases were self-employed and were engaged in their own business (N=66; 13%), without significant differences between gender in this group (Male 19 and female 17).

Table: 4: Distribution of Patient according ICD-10 Diagnosis

Diagnosis	Percentage	Number
F0	1.56%	8
F10	2.94 %	15
F20	10.98%	56
F30	32.94%	168
F40	41.96%	214
F50	1.56%	8
F60	0.19%	1
F70	5.09%	26
F80	0.39%	2
F90	2.35%	12

This study reveals that 214 (41.96%) were suffering from the Neurotic, stress related and somatoform disorders, whereas 168 (33.06%) from mood disorders and 56 (10.98) from schizophrenia and related disorders (Table 4). There were significant less number of patients with diagnosis of F 60 and 80.

Discussion:

Present study showed that most of the patient who have been attending the psychiatric Out-patient Department of Nobel Medical College Teaching Hospital are suffering from neurotic, stress-related and somatoform disorders (41.96%), which was followed by mood disorders (33.06%), schizophrenia, schizotypal and related disorders (10.98%) and mental and behavioural disorders due to use of psychoactive substances. Our findings are similar to the findings reported by Nepal et al (1986)[5], who reported neurotic and related

disorders (anxiety neurosis, [12.7%], adjustment disorder [2%], hysterical illness [2.7%] and somatisation disorder [2%], as the most common psychiatric disorders in an out-patient department at a tertiary level hospital in Nepal. He also observed depression and Schizophrenia as other two most common psychiatric disorders in an OPD setting, which is consistent with the findings of this present study. However the findings of the present study significantly differs from other studies reported by K.C and Shah, (1986)[4], Wright (1987)[6], Shrestha (1987)[7], and Sharma (1987)[8] whose observation shows significant high proportion of patients with diagnosis of epilepsy psychosis and depression, rather neurotic disorders. Sharma (1987)[8] described 42% of the patients in his study to be suffering from depression, 17% from neurosis and 16% from epilepsy. Similarly Shrestha (1987)[7], reported a vast majority of patients with diagnosis of psychosis (63.7%), which was followed by neurosis (18%) and epilepsy (6%) respectively.

Our findings are also similar to the findings reported by Dube (1970)[9], and Neki[10], who observation revealed that near about 44% of the patients, in a community setting in northern part of India, were suffering from neurotic and related disorders which was followed by schizophrenia (9.1%). Similar results have also been reported in literature by many eminent mental health professionals throughout the world (Choo, 1997[11]; Uys et al, 1995[12],Patel, 1997[13], Thom et al, 1997[14]; and Gureje,2006[15], but they differ in terms of either methodology or diagnostic profiles. The reasons of the difference may be many, and some of them are the cultural factors, literacy rate in the different areas where the studies were conducted, and the setup e.g. psychiatry OPD of a general hospital, community set up, private clinic, mental hospital etc.

Although the present study finds Neurotic, Mood Disorders and Schizophrenia as most common psychiatric disorders amongst the people who have been attending the psychiatric out-patient department of Nobel Medical College Teaching Hospital, there were also a noticeable number of cases who did fulfil the ICD-10 Diagnostic Criteria for organic mental disorders (1.56%), behavioural syndromes associated with physiological disturbances and physical factors (1.56%), disorders of adult personality and behaviour (0.19%), mental retardation (5.09%), disorders of psychological development (0.3%), and behavioural and emotional disorders with onset usually occurring in childhood and adolescence (2.35%). Thus, although the bulk of the patients were suffering from neurotic and affective disorders, the patients suffering from the other disorders were also diagnosed and provided services in the Psychiatry O.P.D. of Nobel medical college, Biratnagar.

Recommendation:

Studies of this nature needs to be regularly conducted. They may not seem ground-breaking in nature, but help in terms of proper planning with resultant improvement in service delivery.

Limitation of Study:

This study is carried out in a OPD setting in a Tertiary Level Teaching Hospital in eastern part of Nepal. Owing to the different socio and cultural parameters, the findings of this study may not likely to be generalized throughout the country; hence the authors therefore would like to propose a separate large scale community and institutionalized based study so that the data can be well generalized.

References:

1. ***World Health Organization***. International Classification of Disease and Related Health Problems- Tenth Revision. Mental and Behavioural Disorders: Clinical Description and Diagnostic Guidelines. Geneva: World Health Organization, 1992

2. ***World Health Organisation*** – investing in Mental Health ,2003

3. ***World Health Organisation***. Quality Improvement for Mental Health. Geneva:World Health Organisation, 2003

4. ***Govinda, KC, & Shah, R***. First 150 patients of a new psychiatric OPD: Socio-demographic profile and their diagnostic status. Journal of Nepal Medical Association, 424(3) 7-19, 1986

5. ***Nepal, MK., Gurung, CK., Jha AK., Govinda, KC, & Shah,R.*** First 150 patients of a new psychiatric OPD: Socio-demographic profile and their diagnostic status. *PJournal of Nepal Medical Association*, 424(3) 7-19, 1986.

6. ***Wright, C***. Community mental health services in Nepal-early experiences. In: Proceedings of the Workshop on National Mental Health Planning, pp. 13-27, Kathmandu, 1987

7. ***Shrestha, NM***. A prospective analysis of 300 cases attending outpatient clinic in Mental Health Clinic. In Proceedings of the Workshop on National Mental Health Planning, pp. 47-73, Kathmandu, 1987

8. ***Sharma, BB***. Socio-demographic analysis of 100 cases seen at Pokhara Mental Health Clinic. In: Proceedings of the Workshop on National Mental Health Planning,74-82, Kathmandu, 1986

9. ***Dube, KC***. A study of prevalence and biosocial variables in mental illness in a rural and urban community in Uttar Pradesh, India. Acta Psychiatrica Scandenevica, 46, 327-359, 1970

10. ***Neki, JS***. Psychiatry in South-East Asia. British Journal of Psychiatry, 123,257-269, 1973

11. ***Choo, CH***. Profile of patients seeking psychiatric treatment from adult public mental health services in Singapore. Annals of Acad Med Singapore ,26,443-448, 1997.

12. ***Uys, LR., Dalmini,NK. & Mabandla, SP***. A profile of selected psychiatric out patients in South Africa. Curatonics, 18(1), 22-25, 1995.

13. ***Patel V. et al***. British Journal of Psychiatry. Volume 171, 60-64, 1997

14. ***Thom RSM, Zwi RM and Reinach SG***. The Prevalence of Psychiatric disorders at a Primary Care Clinic – Soweto, Johannesburg South Africa. Medicine Journal 1993, 83, 653-655

15. ***Gureje O. et a***l. British Journal of Psychiatry, 188, 465-471, 2006

Correspondence Address: ***Naba Raj Koirala,*** Head Department of Psychiatry and Mental Health, Nobel Medical College and Teaching Hospital, Kanchanbari, Biratnagar. E-mail: drnabaraj@yahoo.com

INTERLOCKING INTRAMEDULLARY NAILING IN COMMINUTED FEMORAL SHAFT FRACTURES.

Abul Kalam Mohammad, Ram Kewal Shah, Awais Syed, Pradeep Gupta

Abstract:
A prospective study of 20 comminuted femoral fractures, open and close, treated with interlocked intramedullary nailing. The mechanical strength of the nail and less invasive procedure has made the procedure preferable. Short Operative time and less blood loss was seen during surgical procedure. Out of 20 cases , 10 cases were taken from Nepal Medical College, Kathmandu and 10 cases from Nobel Medical College, Biratnagar, during years 2009 to 2011, which had been completed at least six months follow up. Almost all cases were relatively free from long term complication. The results were promising .All fractures healed within 6 months.

Key words: Comminuted femoral shaft Fractures, Interlocked Nail**.**

Introduction:

Fractures of shaft of femur are quite common .The goal of treatment is early return of extremity function usually achieved by reliable fixation of fractures.

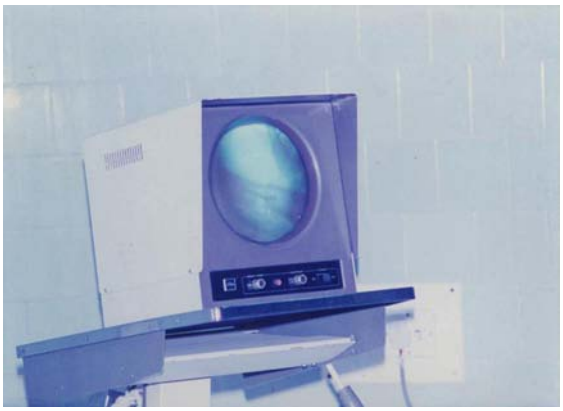
Shortening of the limb and malalignment, along with contractures of the knee due to prolonged immobilization, have traditionally plagued the orthopedist's management of patients who have these injuries.[1, 2].

Treatment goals are reliable anatomic fixation permitting rapid progress out of supine position, early return of extremity function and subsequent restitution of hip and knee motion and strength.

Materials and Methods:

In this prospective study, a total of 20 patients between 20-60 yrs old were treated for comminuted femoral fractures with interlocked intramedullary nailing system. Grade III and IV comminuted[3] fractures and open femoral shaft fractures type I [4] were included. Among these cases, 5 cases were taken from Jan 2009 to June 2009 at Nepal medical college, Kathmandu and 15 cases were from Nobel medical college, Biratnagar from April 2010 to Oct 2011. However comminuted femoral shaft fractures of type I and II, open femoral shaft fractures Type II & III and segmental femoral shaft fractures were excluded. This study only aim to study purely about interlocked nailing system in fracture cases found during study period but not to compare between hospitals results. *Surgical Technique:* All were operated under image intensifier. The patients were put in supine position with the affected side up. A small incision over the greater trochanter area was made and the tip of greater trochanter was exposed and entry point made by using the femoral awl. Using the guide wire and the femur was reamed. The nail of appropriate size was driven slowly. The proximal

interlocking screws were placed through the jig provided with the instrumentation. Distal interlocking screws were placed usually with free hand technique. The final position was checked under the image intensifier. The patients were given intravenous antibiotics.



Position of guide pin being seen in image intensifier

Awl being used to make starter hole in the piriformis fossa

After treatment:

All cases were encouraged to start non weight bearing crutch mobilization after 24 hours of surgery. Gentle range of motion exercises of the knee and hip joints were started on bed. Quadriceps exercises were soon encouraged[5]. Serial X-rays were taken at monthly intervals and gradual weight bearing was started around six weeks after surgery. All cases were followed up for at least six months to be included in the study.

Results:

We had 20 cases of interlocked intramedullary nailing. We have reported the follow-up study up to six months. There were 17 males and 3 female patients with male to female ratio 5.8:1.there were 12 patients in age group 20-29,4 in 30-39, 2 each in age group 40-49 and 50-59.Mean age was 30.6 years in male and 32.5 years in female. (Table 1).

In 75% of cases the fracture was sustained in road traffic accidents especially motorcycle accidents (50%).In 25% of cases firearm was the cause. (Table:2)

There were 8 open fractures, 5 due to firearm and 3 due to road traffic accidents. The rest 12 fractures were close. (Table-3). There was equal number of patients in each Grade III and IV comminution. (Table: 4)

In 6 patients, there were other concomitant injuries and associated medical illness of hypertension or diabetes mellitus was found in 5 patients .These were fairly controlled before surgery was carried out.(table:5).

Most of the fractures took about 18 weeks to heal (60%) while some 5%-10% healed little earlier (table 6) There were a total of 3 (15%) postoperative complications one of each like a knee flexion < 100^0, external rotation of femur 20^0 and shortening of the femur 2 cm. (Table 7)

Table 1: Age and sex distribution (n=20)

Age group	Male	Female
20-29	12	-
30-39	2	2
40-49	1	1
50-59	2	-
Total	17	3

Table 2: Mechanism of injury (n=20)

Mechanism	No. of patients	Percentage
RTA	15	75
Fire arm	5	25

Table 3: Open V/s close fractures (n= 20)

Open v/s Close	Number	Percentage
Close	12	60
open	8	40

Table 4: Extent of comminution (W and H)

Grade	No. of patients'	Percentage
III	10	50
IV	10	50

Table 5: concomitant injuries (6/20, 30%)

Injury	Number	Percentage
Upper limb	1	5
Ipsilateral lower limb	2	10
Contralateral lower limb	1	5
Head injury	1	5
Chest injury	1	5
Total	6	30

Table 6: Fractures healing time (n=20)

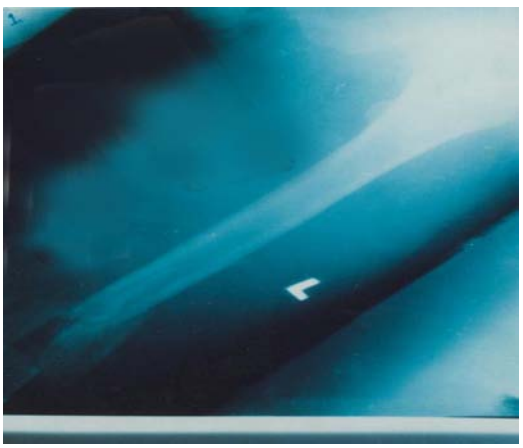
Time in weeks	No. of fractures healed	Percentage
12	1	5
14	2	10
16	2	10
18	12	60
20	1	5
22	1	5
24	1	5
Total	20	100

Table 7: Post of complications (n=20)

Complications	No. of complications	No. of patients	Percentage
Knee Flexion<100^0	1	1	5
External rotation of femur 20^0	1	1	5
Shortening of the femur 2 cm	1	1	5
Total	3	3	15

Discussion:

Interlocked intramedullary nailing system showing excellent result in both close & open fractures. A shorter operative time, less blood loss, easy operative technique, early mobilization, shorter hospital stay and lesser post operative problems. Where ever facilities for interlocked nailing became available, most orthopedic surgeons started treating fractures shaft of femur by interlocked nailing because these system control shortening, angulation & rotation in complex fractures via locking screw.[6,7,8]

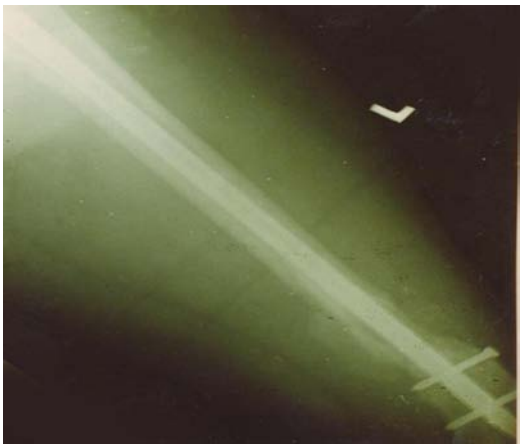


X- ray showing pre operative antro posterior view

X-ray showing immediate post operative lateral view

X-ray showing postoperative antero posterior view

X-ray showing 12 weeks post operative lateral view



X-ray showing 12 weeks post operative antero posterior view

X-ray showing 18 weeks post operative antero posterior view

A deep infection after surgery on the femur is a serious complication. In our study we had no deep infection. In their study the fracture healing time is 17.7 weeks while it was 12 to 32 weeks in the other groups.(table 8)

Table 8: Studies showing fracture healing (interlocking intramedullary nailing)

Studies	Time of healing
Johnson et al(1984)[9]	13.8 weeks
Kempf et al (1985)[10]	17 weeks
Johnson and Greenberg (1987)[11]	14 weeks
Christie et al (1988)[12]	17 weeks
Sojbjerg et al (1990)[13]	12 weeks
Wiss et al (1990)[14]	32 weeks
Anastopoulos et al (1993)[15]	18 weeks
Hajek et al (1993)[16]	12 weeks
Mahmood et al (1993)[17]	32 weeks
Kropfl et al (1995)[18]	14 weeks
Baixuli et al (1998)[19]	20 weeks
Present study	17.7 weeks

Conclusion:

Interlocked Intramedullary Nailing of comminuted femoral shaft fracture is a gold standard method of treatment with advantages of predictability, low rate of complications and full weight bearing is significantly earlier.

References:

1. **Bucholz RW, Jones** A. current concepts review fractures of the shaft of the femur. J Bone joint Surg 1991; 10 (73A):1561-66.
2. **Winquist RA, Hansen ST**. Comminuted fractures of the femoral shaft treated by intramedullary nailing. Orthop clin North Arm 1980; 11(3):633-48.
3. **Winquist RA, Hansen ST Jr, Clawson DK.** Closed intramedullary nailing of femoral fractures: A report of five hundred and twenty cases. J Bone joint Surg 1984; 66A: 529-39
4. **Gustilo RB, Mendoza RM, Williams DN**. Problems in the management of type III(sereve) open fractures: A new classification of type III open fractures. J Trauma 1984; 24: 742-46.
5. **Rockwood CA Jr, Green DP, Bucholz RW, Heckman JD(eds).**Rockwood and Green's Fractures in Adults. 4th Ed. Philadelphia: Lippincott Raven publishers, 1996; 2:1827-1918.
6. Russell TA, Taylor JC, Lavelle DG, Beals NB, Brumfied Dc, Durham AG. Mechanical

characterization of femoral interlocking intramedullary nailing interlocked nailing for treatment of segmental fractures of the femur. J Bone joint Surg 1990; 72A (5):724-28-40

7. **Russell TA.** Biomechanical concepts of femoral intramedullary nailing (Review paper), Intern J orthop Trauma 1991; 1(1): 36-51.3.4.

8. **Thoreson Bo, Alho A, Ekeland A et al** .Interlocking intramedullary nailing in femoral shaft fracture. A report of forty-eight cases. J Bone joint Surg 1985; 67A:1313-20.

9. **Johnson KD, Johnston DWC, Parker B.** comminuted femoral shaft fractures/ treatment by roller traction, cerclage wires and intramedullary nail or an interlocking nail. J bone joint Surg 1984; 66A:12-22.

10. **Kempf, Grosse A, Beck G**. Closed locked intramedullary nailing. Its application to comminuted fractures of the femur.J bone joint Surg 1985; 67A (5); 709-20.

11. **Johnson KD, Greenberg M**. Comminuted femoral shaft fractures. Orthop clin North Am 1987; 18(1): 133-47.

12. **Christie J, Court- brown C, Kinninmonth AWG, Howie CR.** Intramedullary locking nails in the management of femoral shaft fractures, J Bone joint Surg (Br)1988;70B 206-10.

13. **Sojbjerg J, EiskjaerS. Larsen FM**. Locked Nailing of comminuted and unstable fractures of the femur. J Bone joint Surg 1990; 72 B (1): 23-25.

14. **Anastopoulos G,Asimakopoulos** A ,Exarchou E Pantazopoulous T, closed interlocked nailing in comminuted and segmentel femoral shaft fractures J. trauma 1993;35(5):772-75

15. **Hajek PD, Bicknell HR, Bronson WE, Albright JA, SahaS,** Louisiana S. The use of one compared with two distal screws in the treatment of femoral shaft fractures with interlocking intramedullary nailing: A clinical and biomechanical analysis. J bone joint Surg 1993; 75A (4):519-25.

16. **Mahmood R,Shah AA, Shah GA, Chatha M, Sultan S.** Closed intramedullary nailing of femoral shaft fractures. J Pak Orthop Assoc 1993;2(7):16-18

17. **Mahmood R,Shah AA, Shah GA, Chatha M, Sultan S.** Closed intramedullary nailing of femoral shaft fractures. J Pak Orthop Assoc 1993;2(7):16-18

18. **Kropfl A, Naglik H, Primaveri C Hertz H.** Unreamed intramedullary nailing of femoral fractures.J Trauma 1995; 38(5):717-26.

19. **Baixauli F Sr, Baixauli EJ, Sanhez Alepuz E, Baixauli F Jr.** Interlocked intramedullary nailing for treatment of open femoral shaft fractures. Clin orthop Related Res 1998;350:67-73

Correspondence Address: **Dr. Abul Kalam Mohammad**, Department of Orthopedics, Nobel Medical College and Teaching Hospital, Kanchanbari-5, Bitatnagar.

EVALUATION OF CHRONIC HEADACHE BY COMPUTED TOMOGRAPHY: A RETROSPECTIVE STUDY

Anish Subedee

Abstract:

Objective: To find out the proportion of intracranial abnormalities in patients with chronic headache without neurologic abnormality with the use of computed tomography (CT) and to compare the results with similar studies done previously.

Materials and methods: CT images of 56 patients with chronic/recurrent headache and normal neurological findings were reviewed retrospectively. In 38 of 56 patients, both plain and contrast enhanced CT were done. Patients were divided into three groups according to the CT findings: those with no abnormality, those with minor abnormality (that did not alter patient management) and those with clinically significant abnormality. Proportion of patients in each group was found out and results were compared with previous studies with similar study design. Z test was used to evaluate whether the difference in proportions of patients in our study and previous study was statistically significant or not.

Results: Of the 56 patients, 50 had normal CT (89.28 %), four had minor abnormality (7.14%) that did not alter patient management and two had significant lesions (3.57%). Contrast enhanced CT did not improve lesion detection. The minor findings detected were sub-ependymal calcifications of Tuberous sclerosis, calcified neurocysticercosis and old lacunar infarctions in external capsule. Clinically significant lesions detected were small ring enhancing lesion (neurocysticercosis or tuberculoma) and pineal cyst. Results of this study were compared with previous study with similar study design. The Z test showed that the difference in proportions in these studies was not statistically significant ($p = 0.0708$ for minor findings and $p = 0.2033$ for significant findings).

Conclusion: The proportion of intracranial abnormalities detected by CT in this study was similar to that of previous studies. The use of intravenous contrast material administration did not improve its yield. This corroborates the evidence that the ability of CT scan in detecting significant intracranial pathology is poor in patients with chronic headache without neurologic abnormality.

Key words: Chronic headache, CT

Introduction:

Headache is an almost universal experience and one of the most common symptoms in medical practice. It varies from an infrequent and trivial nuisance to a pointer to serious disease (1). Population based estimates suggest that about 4% of adults have daily or near daily headache (2). Although majority of the patients who present with chronic or recurrent headache have no neurologic abnormality, many patients undergo evaluation with computed tomography (CT) and more recently,

magnetic resonance imaging (MRI) to exclude important abnormalities (3).

The studies that have been done so far show that CT is of extremely low yield in patients who undergo imaging for chronic headache without neurologic abnormality (4-6). MR imaging, which is more sensitive than CT in detecting intracranial abnormality (7), has also been found to be unrewarding in evaluation of chronic or recurrent headache without neurological abnormality (3).Yet patient's demand for thorough and high-tech evaluation coupled with the low threshold among doctors for requesting these investigations has accelerated the use of CT and MRI despite the evidences against their use.

Due to unavailability and higher cost of MRI, CT is requested more frequently in our set up. However no data exist in our country about the use of CT for evaluation of chronic headache and normal neurological finding. Thus, the purpose of this study was to evaluate the ability of CT in evaluation of chronic headache without neurologic abnormality. Specifically, this study aimed to find out the proportion of intracranial abnormalities in this group of patient and compare the results with similar studies done previously.

Materials and methods:

Setting: The study was carried out at department of radiology in Chitwan Medical College Teaching Hospital, Bharatpur, Nepal.

- The clinical data and the CT images of the patients undergoing cranial CT scan for the evaluation of chronic headache were retrospectively reviewed.
- Clinical information was collected from the requisition form supplied by the referring doctor. CT images were reviewed from the digital archive of the department.
- All the patients with the chief complaint of chronic / recurrent / long standing headache were included in the study. Exclusion criteria were as follows:
- Inadequately filled requisition forms
- Presence of other neurologic symptoms like trauma, seizures.
- Abnormal neurological finding in clinical examination.
- Patients with diagnosed CNS abnormality
- Of the consecutive 515 head CT scans done between 2009-04-28 and 2009-10-01, only 56 scans were included in the study.

CT scan: All the patients underwent scan with same 16 slice CT scanner (Bright speed, GE). Helical scan of the cranium from base of the skull to the vertex was done with collimation of 5 mm and multi-planar reconstruction at 0.6mm thickness when desirable. Although no definite departmental protocols were present for indication of intravenous contrast material administration, both plain and contrast enhanced scans were done in 38 patients when referring doctor or radiologist recommended its use.

All the images were interpreted by the same radiologist and the imaging results were divided into three groups:

i) those with no abnormality (normal scans)
ii) those with minor abnormality (that did not alter patient management)
iii) those with clinically significant abnormality (which may result in chronic/recurrent headache)

Results:

Of the total 789 CT scans done during the study period, 515 scans (65.27%) were that of head and only 56 patients were included in the study. Of the 56 patients, 16 were male and 40 were female and the age range was 5-72 years.

Of the 56 patients, 50 had normal CT (89.28 %), 4 had minor abnormality (7.14%) that did not alter patient management and 2 had significant lesions (3.57%). Of the patients with minor findings, one had sub-ependymal calcifications of Tuberous Sclerosis, two had calcified neurocysticercosis and one had old lacunar infarctions in b/l external capsule. Two minor findings were seen in male and two in female group. Of the significant findings detected, one was a small ring enhancing lesion (either neurocysticercosis or tuberculoma) in a 12 years girl and another was a pineal cyst measuring 14 mm in diameter in a 30 years female.

The results of present study were compared with previous study with similar study design using CT for evaluation of headache. Dumas MD et al (6) had found that of the 402 CT scans 14 (3.48%) revealed minor findings and 4 (0.99%) revealed significant findings. Z test was used to evaluate whether the difference in proportions of patients in our study and the study of Dumas MD et al was statistically significant or not. For minor findings, the Z value was 1.47 (p =0.0708) and for significant findings Z value was 0.83 (p =0.2033). The difference in proportions in these studies was not significant.

Age and sex wise distribution of the disease was not evaluated for statistical significance because of very small number of observations in individual group.

Among the 56 patients, 38 patients had been investigated with both plain and contrast enhanced CT scans. Of these, none of patients showed additional advantage of contrast enhanced over plain CT. Statistical significance was not evaluated because of small number of patients and number of observations in one of the column being zero.

Table 1: Age distribution:

Age	No. of patients
<20	11
20-39	29
40-59	13
≥60	3

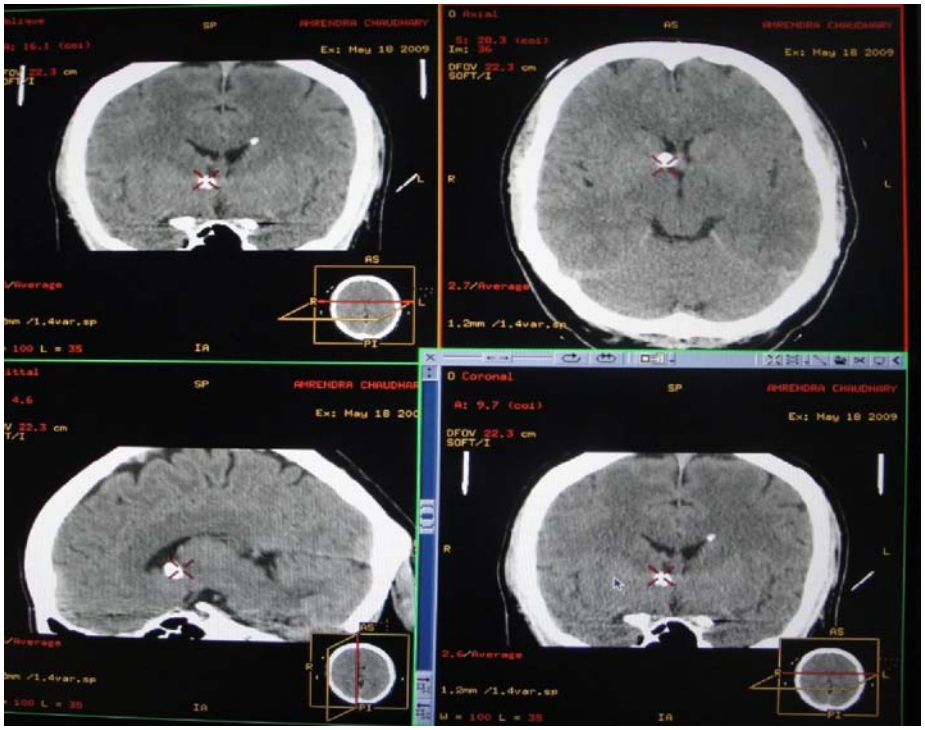


Fig 1: Sub-ependymal calcifications in Tuberous Sclerosis

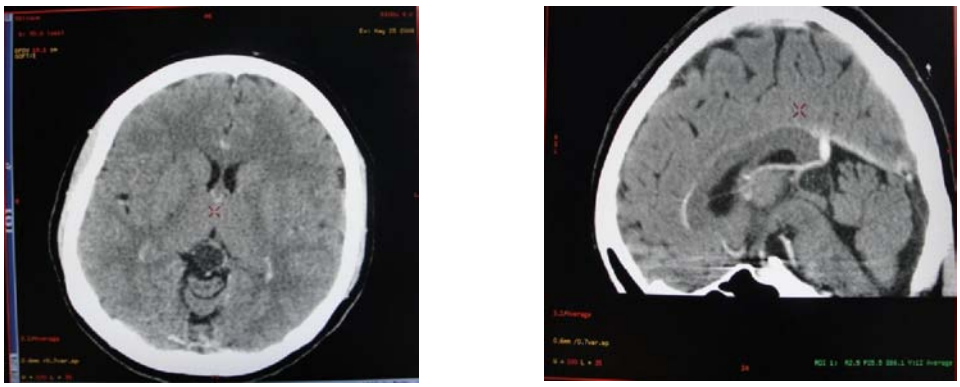


Fig 2: Pineal cyst

Discussion:

In evaluation of chronic headache without neurological abnormality, balancing patient's concern and available evidences regarding use of neuroimaging has been a tight rope walk for clinicians. In practice however tendency towards liberal use of imaging is prevalent. American Academy of Neurology in 2000 had published practice guidelines for imaging in headache (8). Neuroimaging recommendations for non-acute headache are as follows:

Consider neuroimaging in:

- Patients with an unexplained abnormal finding on the neurologic examination (Grade B)

- Patients with atypical headache features or headaches that do not fulfill the strict definition of migraine or other primary headache disorder (or have some additional risk factor, such as immune deficiency), when a lower threshold for neuroimaging may be applied (Grade C)

- Neuroimaging is not usually warranted in patients with migraine and a normal neurologic examination (Grade B).

- No evidence-based recommendations are established for the following:

- Presence or absence of neurologic symptoms (Grade C) Tension-type headache (Grade C)

The US headache consortium (9) later said that the evidences were insufficient to define the role of neuroimaging in evaluation of chronic or recurrent headaches without neurological abnormality. However it made similar recommendations as that of American Academy of Neurology and further recommended larger study involving more than 1000 patients to settle the issue.

Various studies have been done to evaluate the ability of neuro-imaging in detecting abnormalities in patients with chronic or recurrent headache without neurological abnormality. Definition of minor and significant abnormality however was not uniform among the studies performed earlier. Only two studies were found having study design similar to our study, one using CT and another using MR imaging for evaluation of headache. Hence the results of present study were compared only with the study of Dumas et al who had used CT for evaluation of headache.

The present study found that 7.14% of patients had minor abnormality and 3.57% had significant abnormality mandating change in line of management. Presence of pineal cyst was taken as significant on the basis of a study conducted at Germany (10) in 51 patients with pineal cysts which showed significant causal relationship between pineal cyst and headache. Comparison of proportions of patients with minor and significant abnormality with prior study showed no significant statistical difference (6).

Other studies also showed results similar to our study. According to a meta-analysis (9), significant clinical abnormalities detected in CT scans in patients with unspecified headache ranged from 0.0% to 6.7% in ten studies. Though MR imaging is considered more sensitive than CT, one study done in Japan concluded that MR is an unrewarding technique in evaluation of patients with chronic or recurrent headache and neurologic findings (3).

Value of intravenous contrast material administration in this group of patient has also been evaluated previously by different authors (11,12). None of the studies have shown value of contrast material administration in this group of patient which is similar to our findings. Moreover contrast administration means additional cost to the patient along with the risk of adverse drug reactions as well.

Some of the previous studies have tried to evaluate the cost effectiveness of CT scan in this group of patient (6,13). Both show very high cost per single significant finding. CT scan is one of the expensive investigations in our country also. Its use in evaluation of a

problem which is universal in magnitude especially when the diagnostic yield is so little should be seriously re-evaluated in underdeveloped country like Nepal.

Many patients seek attention for their headache because of the anxiety that they are having significant intracranial disease. It has been argued that the relief patient feels that he/she does not have any significant intracranial disease is a worthwhile outcome. However anxiety relief is subjective and difficult to measure. Furthermore, patients prone to anxiety may not feel completely relieved even after undergoing CT scan.

There were few important limitations of this study. First, lack of records of neurological evaluation was an important limitation which might have misled us in patient selection. Our study being retrospective in nature, and most of the patients coming from out patient department, record of complete neurological evaluation could not be obtained. Second, small number of patients in the study was another limitation. The number of patients in individual sub group, in which patients were categorized according to their imaging findings, was subsequently very small.

Conclusion:

In the patients with chronic/recurrent headache without neurologic abnormality, CT detected minor abnormalities in 7.14% and significant abnormalities in 3.57% of patients. The use of intravenous contrast material administration did not improve its yield. This result is consistent with findings of previous studies. This further corroborates the evidence that the ability of CT scan in detecting significant intracranial pathology is poor in this group of patients. However large studies need to be done to establish the role of CT scan in evaluation of the patients with chronic headache.

References:

1. **Clarke CRA.** Neurological Disease. In: Kumar P, Clark M, editors. Clinical Medicine. Sixth ed. Elsevier Limited; 2005. p. 1174.
2. **Goadsby PJ, Raskin NH. Headache**. In: Fauci AS, Braunwald EB, Casper DL et al, editors. Harrison's Principles of Internal Medicine. 17th ed. McGraw Hill Medical; 2008. p. 103.
3. **Tsushima Y, Endo K**. MR imaging in the evaluation of chronic or recurrent headache. Radiology 2005; 235:575-579.
4. **Practice parameter**: the utility of neuroimaging in the evaluation of headache in patients with normal neurological examinations (summary statement). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 1994; 44:1353-1354.
5. **Frishberg BM**. The utility of neuroimaging in the evaluation of headache in patients with normal neurologic examinations. Neurology 1994; 44: 1191-1197.
6. **Dumas MD, Pexman JH, Kreeft JH**. Computed tomography evaluation of patients with chronic headache. [pulished correction appears in Can Med Assoc J. 1995; 152:158]. CMAJ 1994; 151:1447-1452.
7. **Haughton VM, Rimm AA, Sobocinski KA, et al.** A blinded clinical comparison of MR imaging and CT in neuroradiology. Radiology1986; 160:751–755.
8. **Practice parameter:** Evidence-based guidelines for migraine headache (an evidence based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 1994; 44:1353-1354.
9. **Frishberg BM, Rosenberg JH, Matchar DB, et al.** Evidence-based guideline in the primary care setting: neuroimaging in patients with nonacute headache. U.S. Headache Consortium Web site. Available at: www.aan.com.
10. **Seifert CL, Woeller A, Valet M, et al. Headaches and pineal cyst:** a case control study. Headache 2008 Mar; 48(3):448-452.
11. **Jordan JE, Ramirez GF, Bradley WG, Chen DY, Lightfoote JB, Song A.** Economic and outcomes assessment of magnetic resonance

imaging in the evaluation of headache. J Natl Med Assoc 2000; 92:573–578.

12. **Osborn RE, Alder DC, Mitchell CS.** MR imaging of the brain in patients with migraine headaches. AJNR Am J Neuroradiol 1991; 12:521–524.
13. **Kahn CE Jr, Sanders GD, Lyons EA et al.** Computed tomography for non-traumatic headache: current utilization and cost effectiveness. Can Assoc Radiol J. 1993 Jun; 44(3):189-193.

Correspondence Address: **Anish Subedee**, Lecturer and Consultant Radiologist, Department of Radiology, Nobel medical College Teaching Hospital, Biratnagar-5, Nepal. E-mail: anish_subedee@yahoo.com

STATUS OF THYROID PROFILE IN TYPE-2 DIABETES MELLITUS

Shekhar Chandra Yadav, Alwin Saldhana and Biswajit Majumdar

Abstract:

Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemia resulting from defect in insulin secretion and/or insulin action. Thyroid dysfunction in diabetes mellitus patient has been frequently encountered. The clinical relationship between diabetes mellitus and thyroid function is becoming more widely recognized with hypothyroidism among diabetes mellitus patient. Total of 100 cases and 50 controls are enrolled into the study. Their fasting venous blood sample was taken and analyzed for blood sugar, T3, T4 and TSH. Blood sugar and TSH level were elevated while T3 and T4 level were statically decreased in case group in comparison to control group.

Key Words: Diabetes mellitus, hypothyroidism

Introduction:

Diabetes is regarded as single disease entity. Diabetes is a heterogeneous group of diseases characterized by chronic hyperglycemia resulting from diverse group of etiology such as environmental and genetic factors acting simultaneously or jointly.

The cause of Diabetes Mellitus is defective production of Insulin or defective action of Insulin, a hormone that controls the metabolism of carbohydrates, proteins and lipids. Diabetes is regarded as long term disease without variable clinical manifestation and progression of diseases. Chronic hyperglycemia from any route of cause leads to dyslipidemia, hypothyroidism and elevated thyroid stimulating hormone, cardiovascular diseases, renal diseases, neurological problems and recurrent infections.[1]

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia resulting from defect in Insulin secretion and Insulin action or both. Thyroid dysfunction in diabetes mellitus patients has been frequently encountered. The clinical relationship between Diabetes Mellitus and thyroid functions is becoming more widely recognized with hypothyroidism among diabetes mellitus patients.[2]

Diabetes is a "the bergh" disease affecting at least 20 million people throughout the world. Its prevalence in adult population is 2-5%. In some developing countries such as Philippines, the disease prevalence is increasing rapidly due to rapid change in life style. IDDM effect 1 to 500 children and 1 in 200 adolescence.[3]

Type 2 diabetes mellitus, epidemic in Indian is a result of social influence and changing life style. Epidemiological study in the 1960s and 1970s using random and post load glucose estimation reported diabetes prevalence varying from 1-4% in the urban population and 1-2% the rural population and more standardize epidemiological study in 1990's reported prevalence rate that vary from 5-15% among urban population, 4-6%

in the semi-urban population and 1 –5% in rural population.[4]

Thyroid dysfunction:

Thyroid and thyroid dysfunction:

Thyroid gland is unique among the organ of endocrine system because of its size and superficial location. It consists of two bulky lateral lobes connected by a relatively thin isthmus usually located below and anterior to the pharynx. The weight of normal adult thyroid is approximately 15-20 gm. The thyroid has rich intra glandular capillary network that is supplied by the superior inferior thyroid arteries.

The major hormone secreted is T3 and T4. Hyperthyroidism and hypothyroidism are two primary pathological conditions that involve the thyroid gland.[5]

There are few studies on type-2 diabetes mellitus and thyroid dysfunction. They seem to indicate an assurance of thyroid dysfunction among diabetic when compared to the general population (12.7%) where hypothyroidism is the most common type of dysfunction. They found no significant difference between patient thyroid profile and that of euthyroid patient with type-2 diabetes mellitus. The highest percentage of patient whose thyroid dysfunction was diagnosed may justify routine thyroid function assessment of type-2 diabetes mellitus.[6]

Material and Method:

The present study was carried out on total 150 subjects. subjects were divided into two groups. First case group which consist of 100 subjects with known type-2 diabetes mellitus. And second control group which consist of 50 subjects who had no complain and history of diabetes and any thyroid disease.

Twelve hours overnight fasting venous blood sample collected from these subject in fluoride and heparin vacutainer and samples were centrifuged for the estimation of Fasting Blood Sugar (FBS), T3, T4 and Thyroid Stimulating Hormone (TSH).

Sample was analyzed by using biochemistry autoanalyzer. BS-300 chemistry analyzer (Mindray) for analysis of fasting blood sugar and Advia centaur CB immunoassay system (By Bayer) for analysis of hormones T3, T4 and TSH. FBS was estimated by GOD-POD, Enzymatic photometric method while Chemiluminiscence method was used to estimate the levels of T3, T4 and TSH.

Results:

Present study analysed the fasting blood sugar and thyroid profile (T3,T4 and TSH) in Type-2 diabetes mellitus compared with control population. In this study two groups population was there; case group (51 male & 49 female) and control group (26 male & 24 female) having similar age and sex. The mean standard deviation of age and sex of case and control group is statically insignificant, shown in table 1. The P value is 0.270of age and sex distribution of the study. The personal history consisting of diet, use of alcohol along with family history of the subjects was recorded.

In the thyroid profile T3 and T4 level is statically reduced in case group compare to control group which is shown in table 3 with P value less than 0.001 respectively

But TSH value statically increased in case group compare to control group which is shown in table 3 and P value is 0.001. The level of fasting blood sugar is statically

elevated in case group compare to control group (P value is less than 0.001) which is shown in table 3.

Table 1: Age distribution of subjects studied

Age in years	*Controls*		*Cases*	
	No	*%*	*No*	*%*
Up to 30 years	1	2.0	1	1.0
31-40 years	12	24.0	19	19.0
41-50 years	22	44.0	35	35.0
51-60 years	7	14.0	28	28.0
61-70 years	6	12.0	13	13.0
>70 years	2	4.0	6	6.0
Total	50	100.0	100	100.0
Mean ± SD	49.24±11.01		51.34±10.92	

Samples are age matched with P=0.270

Figure1: Age distribution of subjects studied

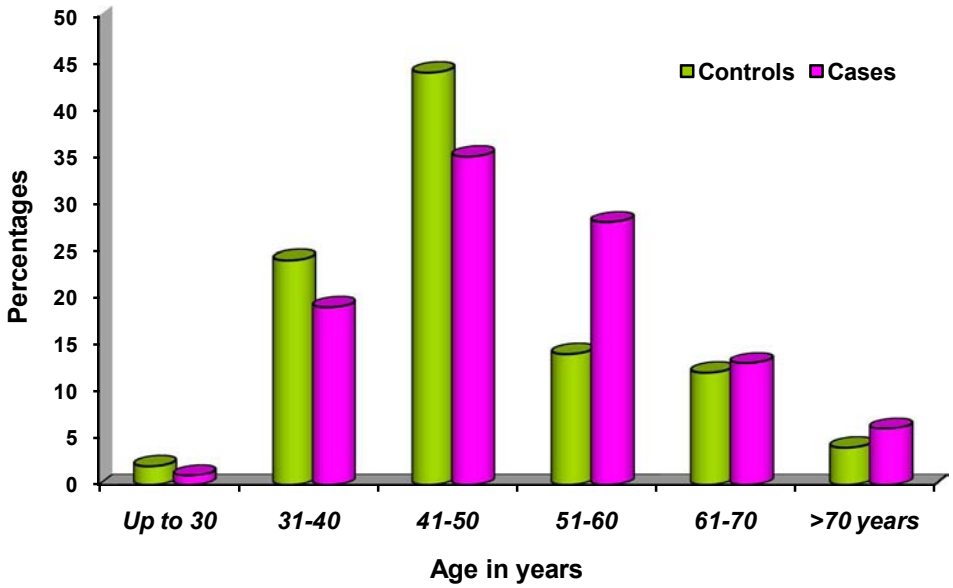


Table 2: Gender distribution of subjects studied

Gender Table 2: Gender distribution of subjects studied	*Controls*		*Cases*	
	No	*%*	*No*	*%*
Male	26	52.0	51	51.0
Female	24	48.0	49	49.0
Total	50	100.0	100	100.0

Samples are gender matched with P=0.908

Figure 2: Gender distribution of subjects studied

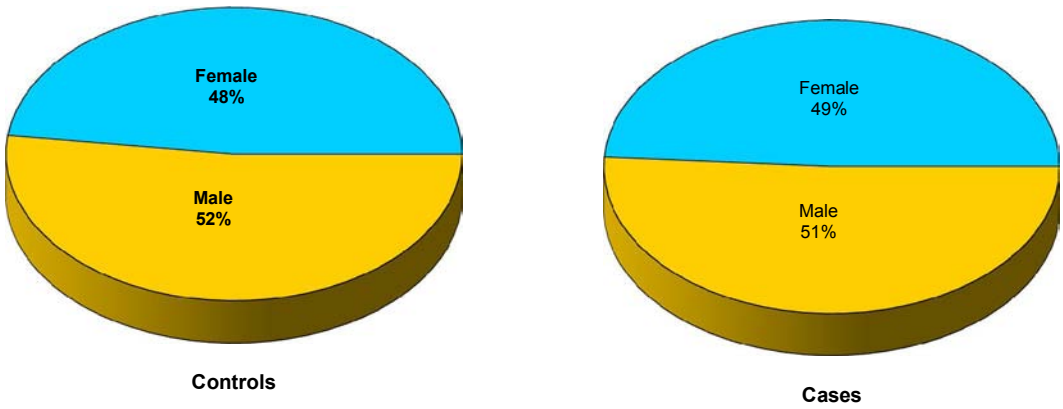


Table 3: Comparison of levels of sugar and thyroid parameters Between controls and cases

Parameters	Controls	Cases	P value	Effect size
FBS (mg/dl)	91.14±9.46 (63-109)	160.75±44.93 (112-350)	<0.001**	1.86 (VL)
T3	1.49±0.26 (0.91-2.00)	0.60±0.44 (0.01-2.00)	<0.001**	2.27 (VL)
T4	7.82±2.49 (3.40-12.30)	3.79±1.92 (0.20-11.20)	<0.001**	1.89 (VL)
TSH	2.89±1.33 (0.35-6.06)	10.38±7.73 (3.90-62.45)	<0.001**	1.17(L)

Results are presented in Mean ± SD (Min-Max). M: Moderate; L:Large;VL:Very large effect

Figure 3: Comparison of levels of sugar parameters between controls and cases

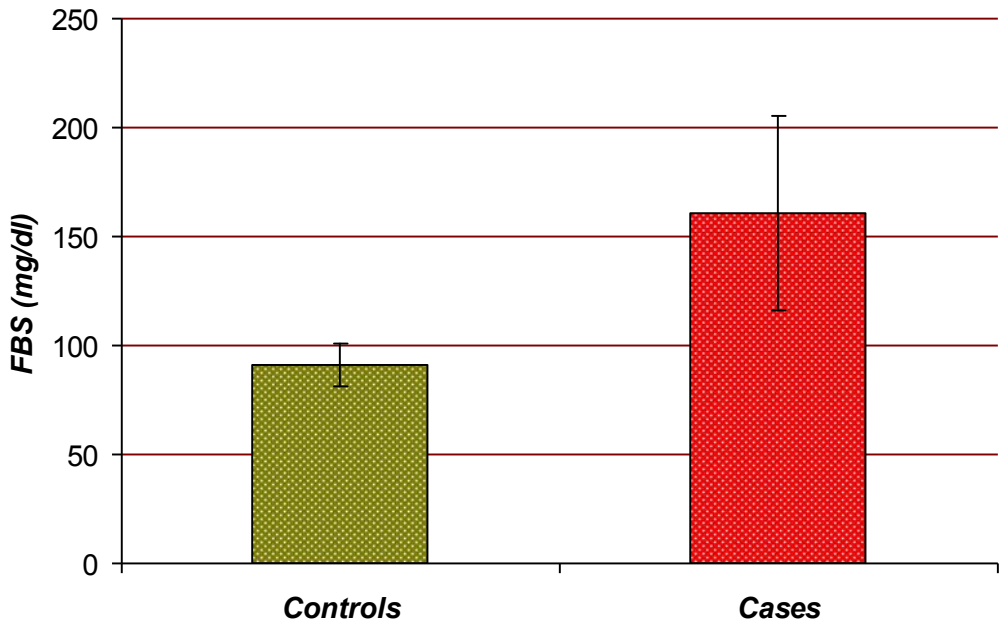


Figure 4A: Comparison of levels of T3 between controls and cases

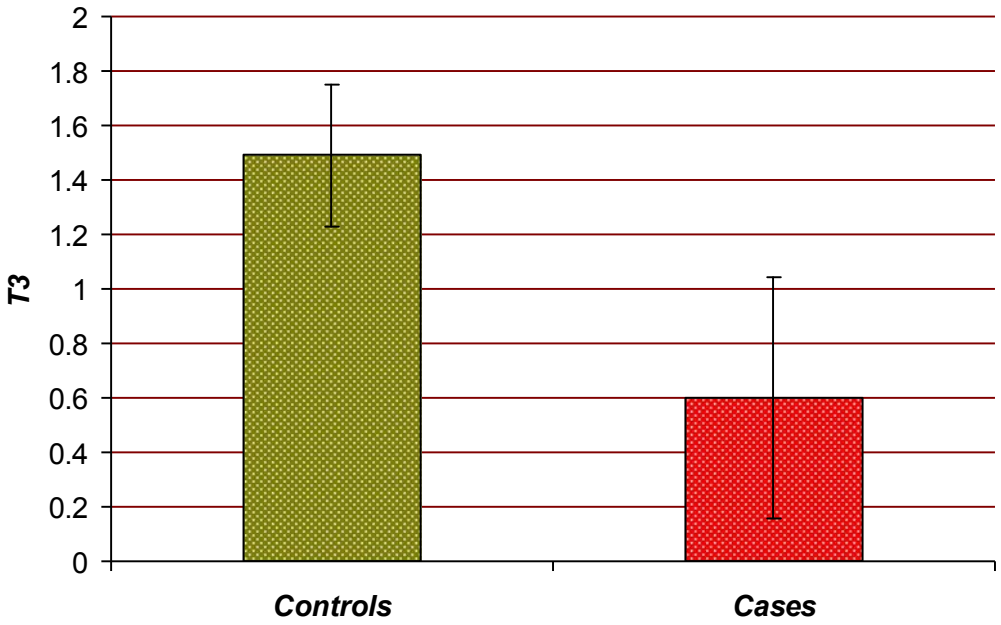


Figure 4B: Comparison of levels of T4 between controls and cases

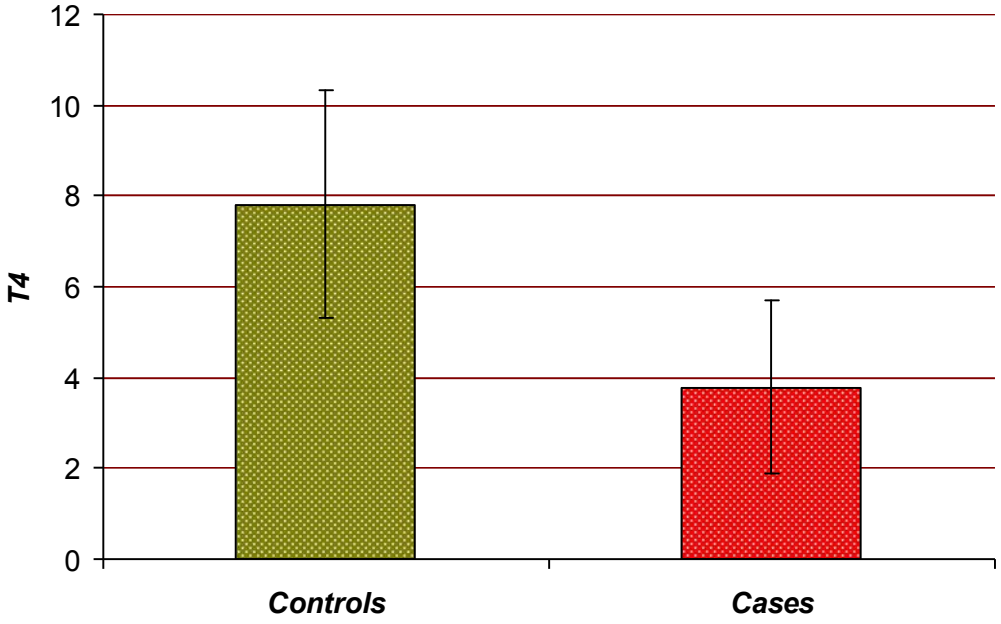
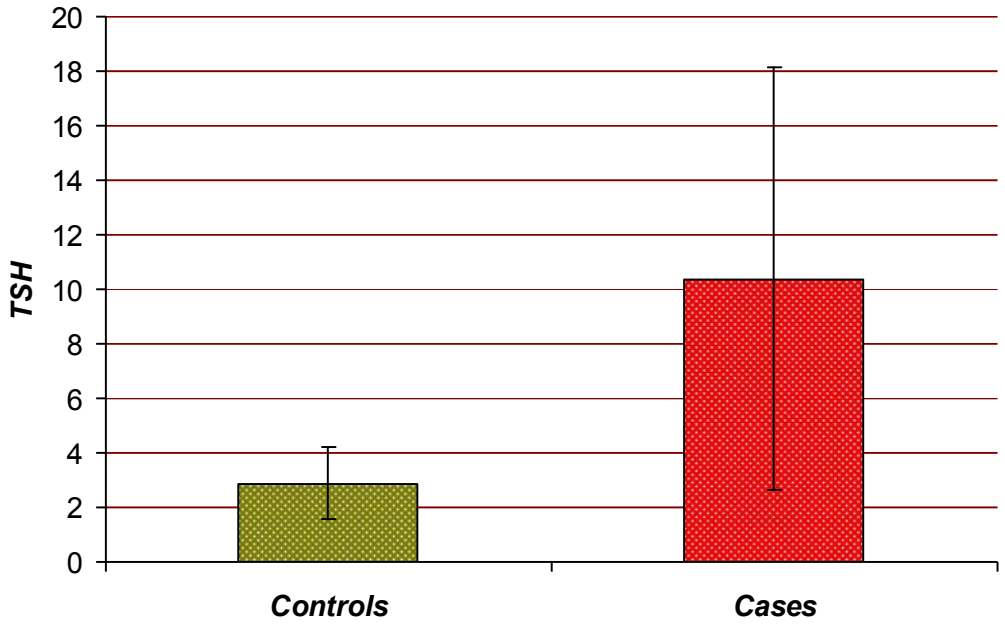


Figure 4C: Comparison of levels of TSH between Controls and cases



Discussion:

The thyroid hormones, tri-iodothyronine and tetraiodothynine are insulin antagonists that also potentiate the action of insulin indirectly TRH synthesis decreases in diabetes mellitus . These facts could be responsible for the occurrences of low thyroid hormone levels in some diabetics. The level of TSH in our study was clinically significant in diabetics than in non-diabetics .Result obtained from present study has shown that in type-2 diabetes mellitus, hypothyroidism, which is a better index to monitor type-2 diabetes mellitus, is frequently observed.[7]

In the present study the distribution of age and sex is matching in control and case group. The fasting blood sugar level were elevated in the case group compare to control group which correlates with the results reported earlier [8,9.10,]

Failure to recognize the presence of these abnormal thyroid hormone levels in diabetics may be a primary cause of poor management often encountered in some treated diabetics. There is therefore need for routine assay of thyroid hormone on diabetics, particularly those whose conditions are difficult to manage.

References:

1. **WHO** 1985 Diabetes mellitus Tecfh.Rep.Ser.No.646.
2. **Process S, Delrange E, Vander Borgh T.V., Jamart T, Donckiet JE.** Minor alteration in thyroid function test associated with Diabetes mellitus and obesity in outpatient without know thyroid illness". Acta Clin.Blg,. 2001 March April.
3. **WHO**. 1985. Diabetes Mellitus. Tech.Rep.ser.No. 727.
4. **Rajeev Gupta and Anoop Mishra**, Author information, "Type-2 diabetes in Indian;

Regional Disparities"; Dr. J Diabetes Vasc Dis.2007;7(1):12-16.

5. **Barzel, US**: thyroid decrease after the sixth decade. Curr Ther Endocrinol metab 1997;6:134-137.
6. **EL Nobre, Z jorge, S prates, C silva and JJ Castro.** Profile of thyroid function in a population with type-2 diabetes mellitus"; British endocrine societies, Abstract; 3:P 298
7. **David, M. and Ath, MD.** Initial management of glycemia in type-2 diabetes mellitus" NEJM, 202; 347(17):1342-1349
8. **Bhalla. K, Shukla. R, Gupta. V.P, Pugazhenthi. S. Prabhu. K.M.** Glycated protein and serum lipid profile in complicated and uncomplicated NIDDM patient" Ind. J.Clin Biochem.1995, 10:57-6
9. **Yegin. A. and Ozben. T.** Serum glucated lipoproteins in type-2 diabetes patient with and without complication" Ann. Clin Biochem." 199, 32:459-463
10. **Panteghini. M, Cimino, A, Pagani. F, Girelli. A.** Nonenzymic glycation of apolipoprotein B in patient with insulin and non-insulin dependent diabetes mellitus" Clin Biochem 1995, 28:587-592

Adress of Correspondance: **Shekhar Chandra Yadav**, Lecturer, Department of Biochemistry, Nobel Medical College, Biratnagar.E-mail:luv4sunrise@yahoo.com

RISING RATE OF CESAREAN SECTION - A YEAR REVIEW.

Shanti Subedi

Abstract:

Caesarean section is one of the most common surgeries performed in modern obstetrics. The rising trend of caesarean section in modern obstetrics is a major concern in health care system all over the world. With all the limited health care resources in a developing country like Nepal, this rising trend definitely has major implication. Rates of caesarean section countries in many countries have increased beyond the recommended level (WHO, 1985). Current available data from developed countries revealed morbidity and mortality from CS is more than in vaginal delivery for both the mother and fetus. Thus this study was conducted to evaluate the rate and indication for CS and to identify the measures to decrease its incidence if possible. Our results shows the foetal distress as the most common indication for Cesarean section in a eastern part of Nepal, which can be minimized significantly if a proper and timly investigation is carried out.

Key words: Caesarean Delivery, Indications, CS audit.

Introduction:

Caesarean section is one of the most common surgeries performed in modern obstetrics. Originally performed in interest of the mother, is now frequently done for foetal indication. Though it was introduced in clinical practice as a life saving procedure both for the mother and the baby. As other procedures of some complexity, its use follow s the health care inequity pattern of the world, underuse in low income setting, and adequate or even unnecessary use in middle and high income setting[1].

Developing countries like Nepal are faced to the challenge of making the best use possible of limited resources to improve the health of women and children. Obstetrical intervention should be evidence based as mortality and morbidity due to unnecessary intervention could be hazardous.

The rising trend of caesarean section in modern obstetrics is a major concern in health care system all over the world[2]. With all the limited health care resources in a developing country like Nepal, this rising trend definitely has major implication. According to WHO, rates of caesarean section in many countries have increased beyond the recommended level of 15%[3], almost doubling in the last decade especially in high income areas like Australia, France, Germany, Italy, North America and United Kingdom[4,5,6,7]. Similar trend is also seen in low resource countries like China, Brazil and India, especially due to births in private hospitals. Eventhough the indication of CS have not changed so far and these remain foetal distress, malpresentation, multiple gestation, previous caesarean, protracted labour and CS on demand. Current available data from developed countries revealed morbidity and mortality from CS is more than in vaginal delivery for both the mother and fetus. Thus this study was conducted to evaluate the rate and indication for CS and to identify the measures to decrease its incidence if possible.

Material and Methods:

This study was carried out in the department of Obstetrics and Gynaecology, Nobel Medical College, Biratnagar, with the aim to analyze the rate and indications for caesarean section. This study also aimed to provide a recommendation for health care professionals which may likely to reduce the rising trend of caesarean section as much as possible. With the objective to fulfil the aforementioned aims, this study was carried out in September 2010 to September 2011. All consecutive patients admitted to the Obstetrics and Gynaecology ward of Nobel Medical College, with history of pregnancy and labor pain, were included in the study. Their demographic details of the patient were recorded including age, parity, address, socioeconomic status, period of gestation, stage of labour and fetal condition.

Results:

A total of 2011 deliveries were conducted in one year, out of which 1560(77.57%) were vaginal,400(19.89%) caesarean and 51 (2.53%) instrumental deliveries (Table 1).Regarding booking status of the patients, it was very low as most of the cases were referred from periphery and government hospital. (Table 2) The various indications of CS were shown in Table 5.

Table: 1: Incidence:

Total Deliveries	2011
Vaginal	1560
Instrumental	51
Caesarean	400

Table 2: Booking Status of the patients

Booked	40
Uunbooked	1971

Table 3: Gravidity Status of the Patients

Primigravida	1400
Multigravida	540
Grandmultigravida	71

Table 4: Types of Cesarean Section

Primary	1926
Repeat	85

Table 5: Indications of Cesarean Section

Indication	***Number (Percentage)***
1. Foetal distress	105 (26.25%)
2. Previous caesarean	85 (21.25%)
3. Failed induction	45 (11.25%)
4. Non-progress of labour	40 (10%)
5. Breech presentation	40 (10%)
6. Cephalopelvic disproportion	16 (4%)
7. Preeclampsia and eclampsia	15 (3.75%)
8. Ante partum haemorrhage	13 (3.25%)
9. Severe Oligohydramnios	10 (2.5%)
10. Multiple pregnancy	10 (2.5%)
11. Obstructed labour	6 (1.5%)
12. Uterine rupture	5 (1.25%)
13. Cord prolapse	5 (1.25%)
14. Caesarean on Demand	5 (1.25%)

Discussion:

In this study the total number of deliveries was 2011 and of which 400 (19.89%) was caesarean deliveries. Increased caesarean rate is a major health concern worldwide, which has increased from 5-7%in 1970 to 25-30% in

2003[8.] Increased rate in developed countries is due to health insurance system, fear of litigation, on demand, extensive use of foetal monitoring. But it is not the rule in our set up as the patients are not given the autonomy of decision making and the health personnel play the key role in patient's decision. Being

a public sector hospital, where safe motherhood programme is implicated it caters a population of low and middle socio-economic class. Our study revealed a CS rate of (19.89%) which is comparable to the rates in different centres like Raipur, India (26.2%), and other South-East Asian countries like The Philippines (22.7%), Malaysia (19.1%), Indonesia (29.6%)[9,10.]. Another study done in tertiary referral centre in Eastern Nepal, BPKIHS revealed a rate of 28.6% in 2006 and 33.7% in 2007[11.] The high CS rate in this hospital may be partially attributed to the fact that this being a referral hospital and it has been hypothesized that increased CS rate may be due to the procedure being performed at a lower threshold of abnormality detection among the

health care providers[12]. The most common indication for CS in our set up was for foetal distress (26.25%).The gold standard method of estimation of foetal distress is not done in our set up and what we have for foetal monitoring is only cardiotocography.CTG is known to overestimate the foetal distress. Many gestational and antepartum factors are known to influence the foetal response in a CTG.The accurate method of estimation of foetal distress is foetal scalp pH estimation[13].

In our study, another common indication was previous CS (21.25%), which is the most common indication worldwide. Enkin et al analyzed a series of 8899 women who were permitted for trial of labour out of them 20.1% were delivered by caesarean section and 79.9%were delivered vaginally[14]. The reluctance to permit a trial of labour after previous CS is probably due to either the obstetrician considering that a repeat CS is much safer and convenient and is less likely to give rise to the complication and possible subsequent litigation or due to maternal preference. In our setup no trial was given even after one previous Cs until and unless women comes in second stage of labour and this is the cause for increased rate for previous CS and failure to conduct VBAC in our hospital was due to lack of trained human resources. Another study done by McMahon et al reported that that higher rates of maternal and foetal morbidity exist with VBAC as compared to repeat CS[15]. However study done by Gonen found that VBAC with a well defined protocol was safe as compared to repeat CS[16].

Failed induction and non-progress of labour were the next frequent indications. Judicious use of oxytocics and the use of partograph are definitely beneficial to reduce the CS rate. Breech presentation accounting for 10% of CS. Though ECV (external cephalic version) has been suggested as an intervention to reduce high CS rate at 37 wks gestation but it has its own drawbacks and requires skill. A meta-analysis showed significantly lower rates of perinatal mortality and neonatal morbidity with planned caesarean section than with planned vaginal birth[17]. .On demand CS rate being 1.25% in our set up. In West countries it is high and comprises of around 23% - 38.9% in the United Kingdom[18].

This trend is also partly due to some evidence that suggests that planned caesarean birth might protect against urinary and faecal incontinence, pelvic organ prolapse and sexual dissatisfaction, further increasing its appea[19].

Conclusion:

The trend in performing caesarean section is increasing and the most common indication for Cesarean section is foetal distress and we should be more investigational to diagnose it as many of the cases didn't have any evidence of it intrapartum.

References:

1. **Luz Gibbons et al**. The Global Numbers and costs of Additionally Needed and Unnecessary Caesarean Sections Performed Per Year: Overuse as a Barrier to Universal Coverage. World Health Report (2010)

2. *Caesarean sections.* Postnote No. 184. London: Parliamentary Office of Science and Technology; 2002. Available from: http://www.parliament.uk /post/pn184.pdf.

3. **World Health Organization**. Appropriate technology for birth. Lancet 1985; 2(8452):436-7.

4**. C Black, JA Kaye, H Jick.** Caesarean delivery in the United Kingdom: time trends in the general practice research database *Obstet Gynecol* 2005; 106: 151-5.

5. **Laws, PJ, Sullivan EA**. *Australia's mothers and*

babies 2002. Perinatal Statistics Series No. 15. Sydney: National Perinatal Statistics Unit; 2004

6. **AL Tranquilli, SR Giannubilo.** Cesarean delivery on maternal request in Italy. *Int J Gynaecol Obstet* 2004; 84: 169-70.

7**. R Dobson.** Caesarean section rate in England and Wales hits 21%. *BMJ* 2001; 323:951

8. Leitch CR.Walkers JJ. Cesarean section rates.BMJ1994; 308:133-4.

9. **Singh Abha and Channawar Reema**. A recent way of evaluating caesarean birth. J Obstet Gynecol IndiaVol. 59, No. 6: November/December 2009 pg 547-51.

10. **Mario R Festin, Malinee Laopaiboon, Porjai Pattanittum, Melissa R Ewens, David J Henderson-Smart, Caroline A Crowther**. Caesarean section in four South East Asian countries: reasons for, rates, associated care practices and health outcomes.BMC Pregnancy and Childbirth 2009, 9:17

11. **S. Chhetri et a**l. Cesarean Section: its rates and indications at a tertiary referral center in Eastern Nepal.2011 September-December 2011; Vol 9(3):179-83

12. **S. N. Mukherjee**. Rising caesarean rate.J. Obstet Gynecol India 2006; (56)4:298-300.

13. **Unnikrishanan B, Rakshith Prasad B et** al. Trends and Indication for Caesarean Section in a tertiary Obstetric Hospital in Coastal South India. AMJ 2010; (821-825).

14. **Enkin M**. Labour and delivery following previous caesarean section. In Enkin M, Keirs MJ,Chalmers I (eds). Elective Care in Pregnancy and Childbirth, pp 1196-1215. Oxford: Oxford University Press, 1989.

15**. Mc Mahon MJ, Luther ER, Bowes WA Jr, Olshan AF.** Comparison of a trial of labor with an elective second caesarean section. N England J Med1996; 335(10):689–

16. **Gonen R, Tamir A, Degani S et al**. Variables associated with successful vaginal birth after one caesarean section: a proposed vaginal birth after Caesarean section score. Am J Perinatol2004; 21:447-53.

17. **Hannah M, Hannah W.** Caesarean section or vaginal birth for breech presentation at term.BMJ1996; 312:1433-1434

18**. Wilkinson C, McIlwaine G, Boulton-Jones C,Cole S.** Is a rising caesarean section rate inevitable?Br J Obstet Gynaecol.1998;105(1):45-52.

19. **Hemminki E, Merilainen J**. Long-term effects of caesarean sections: Ectopic pregnancies and Placental problems. Am J Obstet Gynecol 1996; 174: 1569 -1574.

Correspondence address: ***Shanti Subedi***, Lecturer, Department of Obstetrics and Gynaecology, NMCTH, Biratnagar. Phone no. 9842021806. E-mail: drshantisubedi@yahoo.com

THE PREVALENCE OF MENTAL RETARDATION BY GENDER, AGE, AND AGE OF DIAGNOSIS AT NOBEL MEDICAL COLLEGE, BIRATNAGAR

Naba Raj Koirala, Ajay Kumar, Das and Santosh Kumar Bhagat

Abstract:

Objectives: To evaluate the prevalence of mental retardation by gender and age of diagnosis at Nobel Medical College, Biratnagar.

Methods: The data of all mentally retarded children recorded within a period of one year from 01st May 2011 to 30th April 2012 is analyzed retrospectively. Age, gender, IQ scores, the age of diagnosis, and their living place were evaluated.

Results and conclusion: A total number 103 children attended the Psychiatric Out-patient Department of Nobel medical College and Teaching Hospital over the study period of one year. Out of all those 103 children, 67 children were with normal IQ scores, 7 with coexistence of epilepsy and other medical problems, and 3 children with incomplete case records, thus they were excluded from the study, and the subjects for further study was constituted by just 26 cases, who fulfilled the diagnostic criteria for Mental Retardation according to ICD-10.

The overall prevalence of mental retardation in our study was 25% and the distribution of mental retardation amongst all those 26 cases were as follows: 2 cases (8%) were profound, 3 severe (12%), 7 (27%) were moderate and 9 (35%) mild, and 5 (19%) were borderline. Out of all those 26 mentally retarded children 11 were male (42%) and 15 (58%) were female, and of these cases, 07 were living in urban, and 19 in rural areas. Most of our cases were diagnosed between 6-10 years of age.

Key words: Mental Retardation, Nobel Medical College, IQ Score, Standford-Binet Intelligence scale.

Introduction:

Mental retardation (MR) is one of the most frequent disorders among children. The prevalence rate of MR varies across countries and regions, and this may be attributed to the variations in major classification systems, definitions, and methodologies. Due to these inconsistent criteria, there are considerable variations in the prevalence of MR from 2-85 per 1000.1,2 The diagnosis of MR mainly requires low general intellectual functions and age of onset before the age of 18[1,2]. In addition, deficits in adaptive behavior can also be added as a third component of the traditional definition of MR. The IQ score was the only tool to classify many children as mentally retarded[2,3,4].

The etiologies of MR are multiple, and MR prevalence can also be influenced by social, economic, cultural, racial/ethnic, and other environmental factors including the demographics of age and gender[5,6]. However, epidemiological studies assessing

these relationships are scarce. An association between different forms of MR and social class was first proposed by Lewis[6]. There are many studies that have consistently found that the prevalence of MR was strongly associated with low socioeconomic status[5,6]. In developing countries, the effect of MR on individuals and society has been understudied and there are limited reports from these parts of world although it is likely to be more important. Due to inferior social conditions and limited occupational and educational opportunities, there are some differences in socioeconomic status between rural and urban areas.

The purpose of this study was to estimate the prevalence of MR amongst the children attending the Psychiatric Out-patient Department of Nobel Medical College, Biratnagar, and also to examine the age of diagnosis, gender, and location, of Mental retardation. The age, gender, IQ result, the age of diagnosis, and the location were evaluated in order to establish the differences that might affect the diagnosis and frequency of MR.

Methodology:

Nobel Medical College and teaching Hospital is a tertiary level hospital located in a major economic city in eastern part of Nepal. It provides both in-patient and out-patient services to a large number of patients residing in eastern part of Nepal and also nearby villages in India. All the necessary data for the study was obtained from the Psychiatric OPD of the Nobel Medical College and Teaching Hospital and was analyzed retrospectively. All care takers were informed about the possibility of use of these data in scientific studies and a verbal consent was obtained from them. An Approval was also obtained from the Ethics Committee of the Hospital. There were 103 children attended the psychiatric OPD of Nobel Medical college and Teaching Hospital over a period of one year, 01st May 2011 to 30th April 2012. Out of all those 103 children 67 children were with normal IQ scores, 7 with coexistence of epilepsy and other medical problems, and 3 children with case records that lacked gender, age, age at diagnosis, IQ scores, and/or living areas thus they were excluded from the study living only 15 cases for further analysis. The IQ scores of all those 15 cases were obtained to record the severity of mental retardation according to Stanford-Binet Intelligence Scales, 5th edition (Becker, 2003)[4] as follows: 90-109: Average or Normal; 80-89: Borderline intelligence; 70-79: Mild MR; 50-69: Moderate MR; 20-49: Severe MR; and Below 20: profound. All available data were evaluated by using appropriate descriptive statistical tools.

Results:

In this study, 105 children attended the psychiatric out-patient department of Nobel Medical College and Teaching Hospital over a study period of one year (01st May 2011 to 30th April 2012). Out of all those 103 cases 77 cases were excluded from the study, hence the sample size for the study was comprised by 26 cases, whose intelligence scores on Standford-Binet intelligence scale were below than average, and also fulfilled the diagnostic criteria for mental retardation according to ICD-10.

Table-1; Distribution of Cases according to Gender, Age at first diagnosis, area of living and Scores on Stanford-Binet intelligence Scores (N=26)

Gender	Male = 11 (42%) Female = 15 (58%)
Age at the time of diagnosis	Below 5 years of age = 2 (7.69%) 6-10 Years of age = 13 (50%) 10-15 Years of age = 7 (26.92%) Age above 16 years = 4 (15.38)
Area of Living	Urban = 07 (26.92%) Rural=19 (73.07%)
Scores on Stanford-Binet Intelligence Scales	Profound = 2 (7.69%) (male = 0; female = 2) Severe = 3 (11.53%) (male =1; female = 2) Moderate = 7 (26.92%) (Male = 3; female = 4) Mild = 9 (34.61%) (Male = 4; Female = 5) Borderline = 5 (19.23%) (Male = 3; Female = 2)

In our study Table 1 shows female preponderances over male (15 Vs. 11). Similarly majority of subjects who were diagnosed as cases of mental retardation were living in rural area compared to urban (19 Vs. 07, 73.07% Vs. 26.92%). The age group 6-10 years heavily predominated all other age group in regards to their age when they received the diagnosis of mental retardation first time in their life. Majority of cases according to scores on Stanford-Binet Intelligence scales were found to be suffering from mild (N=9, 34.62%), and that was followed by Moderate level of mental retardation (N=7, 26.92%). The overall prevalence rate of mental retardation in this study was equal to 25%.

Discussion:

Mental retardation (MR) is defined as sub-average general intellectual functioning, which originated during developmental period and is associated with impairment in adaptive behavior. Mental handicap is the present term used for mental retardation. It is a condition of sub-average intellectual function combined with deficits in adaptive behavior. Mentally retarded children are one of the most frequently encountered, and most distressing, disabilities among children in most industrialized and developing countries world-wide[6, 7]. Its prevalence rate varies considerably because of the varying criteria and methods used in the surveys, as well as differences in the age range of the samples, but its overall prevalence is equal to 1-3% among children all over the world[1,2,8]. It is more common in developing countries because of the higher incidence of injuries and anoxia around birth, and early childhood brain infections[9]. Although common amongst children, mental retardation is the most difficult categories of childhood disability to document epidemiologically, in part because its causes are multi-factorial. In less developed countries, like Nepal, the difficulties of documenting the causes of MR are compounded by lack of diagnostic

services and routinely collected health data. Similarly many cases of mild retardation look like normal children and are diagnosed only after scholastic backwardness or failure. The effect of MR on individuals and societies has been underestimated in developing countries, and there are limited reports from this part of world although it is likely to be more important.

Previous studies have consistently shown that individuals from low socioeconomic status and rural areas are over represented among those with mild MR[2,3,5,7,8]. Some investigators have even suggested that mild MR rarely occurs among individuals from the upper socioeconomic groups unless other underlying neurological conditions are present[8]. Unfortunately, comprehensive data on socioeconomic status of individuals in our study does not exist in database. Thus, the status of the patients has been roughly pointed out according to their living area.

It is generally an accepted notion that the annual income of individuals living in the urban area of eastern part of Nepal is higher than the rural area. Data on migration of individuals are also an important issue. However, our record does not include any information on these topics too. However we can extrapolate that the Nobel Medical College and Teaching Hospital is located in Biratnagar, the major economic zone of the country, and the available heath service is largely accessible to those who are living in an urban area, thus preventing many of earlier possible causes of mental retardation in later age. In our study mild MR was established more in the rural population, and this in accordance with previous studies[2, 3, 5, 7, 9, 10, 11, 12]. In addition, the low percentage of borderline cases in our study may also likely to be explained on the ground of cultural variation prevalent in our society, where most of the children mainly male works in laboring jobs or in agriculture and constitutes as a major work force and may easily be ignored[11, 12,13]. This may explain why the borderline MR was lower in our study. The female preponderances over male in our study may also be explained with support of the prevalent culture in the society, where female children are mostly engaged in the domestic works in their earlier age as compared to male and their incapacity at domestic works and later marital life is easily identifiable by the caretakers. In our study, the prevalence rate of mental retardation was 25 percent, and it likely to be matched with other studies reported in the country[2,3, 11,14, 15, 16].

References:

1.**Accordo PJ, Capute AJ.** Mental Retardations. *Ment Retard Dev Disabil Res Rev* 1998; 4: 2-5.

2.**Roeleveld N, Zielhuis GA, Gabreels F**.The prevalence of mental retardation: a critical review of recent literature. *Dev Med Child Neurol* 1997; 39: 125-132.

3.**Kiely M**. The prevalence of mental retardation. *Epidemiol Rev* 1987; 9: 194-218.

4. **Becker, K. A.** Stanford-Binet Intelligence Scales, Fifth Edition. Itasca, IL: Riverside Publishing, 2003.

5.**Croen LA, Grether JK, Selvin S.** The epidemiology of mental retardation of unknown cause. *Pediatrics* 2001; 107: E86.

6.**Drews CD, Yeargin-Allsopp M, Decoufle P, Murphy CC**. Variation in the influence of selected sociodemographic risk factors for mental retardation. *Am J Public Health* 1995; 85: 329-334.

7.**Leonard H, Petterson B, De Klerk N, Zubrick SR, Glasson E, Sanders R, et al.** Association of sociodemographic characteristics of children with intellectual disability in Western Australia. *Soc Sci Med* 2005; 60: 1499-1513.

8.**Stromme P, Magnus P**. Correlations between socioeconomic status, IQ and aetiology in mental retardation: a population based study of Norwegian children. *Soc Psychiatry Psychiatr Epidemiol* 2000; 35: 12-18.

9.**Islam S, Durkin MS, Zaman SS**. Socioeconomic status and the prevalence of mental retardation in

Bangladesh. *Ment Retard* 1993; 31: 412-417.

10.**Fernell E.** Mild mental retardation in schoolchildren in a Swedish suburban

municipality: prevalence and diagnostic aspects. *Acta Paediatr* 1996; 85: 584-588.

11.**Anupam Pokharel, Saroj P. Ojha, Naba Raj Koirala, et al**. A profile of the children and adolescence referred by paediatricians to the child guidance clinic of Tribhuvan University Teaching Hosiptial. *Nepalese Journal of Psychiatry (2001), Vol. 2, No. 4*

12.**Nepal, M.K., Sharma, P. & Gurung, C. K.** The first child psychiatric clinic: an initial appraisal. NEPAS, 7 (1), 71-75, 1988.

13.**Ojha, S. P.** Emotional and Behavioral Problems in physically Disabled Children and Adolescents. MD Thesis, Institute of Medicine, Maharajgung, Kathmandu, 1999.

14.**Regmi, S.K., Khalid, A., Nepal, M.K. & Pokharel, A.** A study of sociodemographic characteristics and diagnostic profile in psychiatric outpatients. *Nepalese Journal of Psychiatry*,1999; 1(1), 26-33.

15.**Regmi, S.K., Nepal, M.K. Khalid, A., Sinha, U.K., Kiljunen, R., Pokharel, A. & Sharma, S.C.** A study of Children and Adolescents attending the Child Guidance Clinic of a General hospital. *Nepalese Journal of Psychiatry*, 2000; 1(2), 90-97.

16.**Shrestha, D.M.** Neuropsychiatric problems in children attending a general psychiatric clinic in Nepal. *Nepal Paediatric Society Journal, 1986*; (1), 97-101.

Correspondence Address: Naba Raj Koirala, Head, Deparment of Psychiatry and Mental Health, Nobel Medical College and Teaching Hospital, kanchanbari-5, Biratnagar, Nepal.

DERMOID CYST OF OVARY MISDIAGNOSED AS INTRAUTERINE FETAL DEMISE: A CASE REPORT

Varsha, Shanti Subedi, Anju Deo, Anjana Sharma, and Sita Ghimire

Abstract:
Thirty two years multipara with amenorrhoea of five months presented with bleeding per vagina for ten days. Clinically and radiologically she was diagnosed with intrauterine fetal demise at 20 weeks period of gestation. She was induced with prostaglandins continuously for seven days. On eighth day of admission features of uterine rupture was present. On laparotomy ruptured huge dermoid cyst with chemical peritonitis was discovered. There was no evidence of pregnancy. We are reporting this case for a rare complication of ruptured dermoid cyst and also to illustrate the importance of clinical assessment.

Keywords: intrauterine fetal demise, ruptured dermoid cyst, chemical peritonitis, ultrasound

Introduction:

Mature cystic teratoma (dermoid cyst) is one of the most common benign ovarian neoplasm discovered during pregnancy (20- 40%).[1,2] They may be responsible for complications such as torsion and rupture. Rupture is rare, but once it has occurred it can cause complications such as chemical peritonitis.[3-5] This case illustrates the unusual complication of ruptured dermoid cyst leading to peritonitis misdiagnosed as intrauterine fetal demise.

Case report:

A multiparous lady of 32 years with amenorrhoea of five months presented with bleeding per vagina for 10 days. Clinically on per abdomen examination 20 weeks size irregular mass was palpated. Ultrasound abdomen showed intrauterine fetal demise (fig.1). She was induced with prostaglandin continously for seven days. On eighth day of admission, patient developed abdominal distension and fetal parts could be palpated. Ultrasound revealed fetal parts outside the uterine cavity and free fluid with internal debris in the peritoneal cavity. With the provisional diagnosis of rupture uterus, exploratory laparotomy was performed. In per operative finding ruptured right ovarian dermoid cyst about 15cm x 15cm (fig.2) and sebaceous marerial was seen in the peritoneal cavity. Left ovarian dermoid measuring 5x5 cm was present. Uterus was normal in size. As uterus and the adnexal structures was densely adhered and dissection of demoid cyst was difficult so total abdominal hysterectomy with bilateral salpingoophorectomy was done. On cut section no fetal parts was seen in the dermoid cyst. Uterine cavity and cervical canal was empty. Post surgery urinary pregnancy test was negative. Histopathology report showed mature cystic teratoma. The final diagnosis was ruptured dermoid cyst with chemical peritonitis.

Discussion:

This case of mature cystic teratoma was confused with pregnancy as patient presented with history of amenorrhoea. Ultrasound report showing intrauterine fetal demise misguided us. Clinically 20 weeks size mass was palpated per abdomen and at 20 weeks period of gestation urinary pregnancy test is usually not done. The complaint of the patient and characteristics of the mass such as position and consistency were confused with pregnancy. Bilateral dermoid cyst is present in

only 10 – 15 % of the cases. Rupture of cyst before or during operation may lead to chemical peritonitis. The incidence of chemical peritonitis after rupture and leakage of cystic fluid is less than 0.5 %.[2] Clement et al and achtari et al reported chemical peritonitis following cystic fluid spillage.[6,7] In our case whether repeated dose of prostaglandin led to rupture of dermoid cyst is still controversial.

Conclusion:

Any abdominal mass should be thoroughly investigated. Ultrasound is not the only diagnostic tool. Clinical assessment is mandatory. Overemphasis on ultrasound sometimes gives erroneous impression leading to erroneous management of the case.

References:

1. **Comerci JT Jr, Licciardi F, Bergh PA, Gregori C, Breen JL**. Mature cystic teratoma: a clinicopathologic evaluation of 517 cases and review of the literature. Obstet Gynecol 1994;84:22-8.
2. **Peterson WF, Prevost EC, Edmunds FT, Hundley JM Jr, Morris FK**. Benign cystic teratomas of the ovary; a clinico-statistical study of 1,007 cases with a review of the literature. Am J Obstet Gynecol 1955;70:368-82.
3. **Stuart GC, Smith JP.** Ruptured benign cystic teratomas mimicking gynecologic malignancy.Gynecol Oncol 1983;16:139-43.
4. **Suprasert P, Khunamornpong S, Siriaunkgul S, Phongnarisorn C, Siriaree S.** Ruptured mature cystic teratomas Mimicking advanced stage ovarian cancer: a report of 2 case study. J Med Assoc Thai 2004;87(12):1522-5.
5. **Phupong V, Sueblinvong T, Triratanachat S.** Ovarian teratoma with diffused peritoneal reactions mimicking advanced ovarian malignancy. Arch Gynecol Obstet 2004;270:189-91.
6. **Clement D, Barranger E, Benchimol Y, Uzan S.** Chemical peritonitis: a rare complication of an iatrogenic ovarian dermoid cyst rupture. Surg. Endosc 2003;17:658.
7. **Achtari C, Genolet PM, Bouzourene H, De Grandi P.** Chemical peritonitis after iatrogenic rupture of a dermoid cyst of the ovary treated by coelioscopy. Apropos of a case and review of the literature. GynakolGeburtshilfliche Rundsch 1998;38(3):146-50.

Fig.1. Ultrasound showing Intra uterine fetal death

Fig.2. Left dermoid cyst of ovary

Correspondence Address: **Varsha**, Lecturer, Department of Obstetrics and Gynecology, Nobel Medical College, Biratnagar, Nepal. E-mail: varshanathani2008@yahoo.com

DYKE-DAVIDOFF-MASSON SYNDROME

Naba Raj Koirala, Roshna Khadka, Manoj Bhattarai, Dibya Tulachan, Ajay Kumar Das, and Jwalanta Poudel

Abstract:

Dyke-Davidoff-Masson Syndrome (DDMS) is characterized by seizures, facial asymmetry, contralateral hemiplegia and mental retardation. The characteristic radiologic features are cerebral hemiatrophy with homolateral hypertrophy of the skull and sinuses. Here we report a case of a 16 years young girl who presented with seizures severe mental retardation and weakness of left upper-limb and on CT brain was diagnosed to have DDMS.

Key words: DDMS, Seizure, mental retardation, Hemiatrophy, hypoplasia, cerebral hemisphere

Introduction:

First description of Dyke-Davidoff-Masson syndrome (DDMS) dates back to 1933, when Dyke, Davidoff and Masson described the plain skull radiographic and pneumatoencephalographic changes in a series of nine patients[1]. Since then only few pediatric cases of DDMS have been reported.

Dyke-Davidoff-Masson syndrome (DDMS) is characterized by seizures, facial asymmetry, contralateral hemiplegia and mental retardation. The characteristic radiologic features are cerebral hemiatrophy with homolateral hypertrophy of the skull and sinuses. Hypoplasia of one cerebral hemisphere (hemiatrophy) is mostly secondary to brain insult in fetal or early childhood period. Hemiatrophy is not frequently encountered in clinical practice. We present here a case of a 16 years young girl who presented with seizures and weakness of left upper-limb and on CT was diagnosed to have DDMS.

Case report:

A 16 years young girl born full term, presented to the psychiatry OPD of Nobel Medical College Teaching Hospital with complaints of seizures for near about past 15 years and weakness in left upper limb since birth. Her seizures were controlled with tablet Phenytion sodium 300 mg/day but now for last 4 months she had seizures even when on regular medication. Neurological examination revealed right-sided spastic hemiparesis, brisk deep tendon reflexes, and extensor plantar response. The baby could not stand without support and speak only monosyllabic words. There was no neurocutaneous marker or asymmetry of face or body. Her head circumference, and visual and hearing capacities were normal, so her cranial nerves. Her hematological profile and cerebrospinal fluid examination were also normal. Her Computed Tomography (CT) scan of head revealed hemiatrophy of left cerebral hemisphere, dilatation of the left lateral ventricle, widening of ipsilateral sulci, a well defined cystic lesion and calvarial expansion on the left side. There was shift of the midline to the left. We made a diagnosis of Dyke-Davidoff-Masson syndrome.

Discussion:

In 1933, Dyke, Davidoff, and Masson described the plain skull radiographic and

pneumatoencephalographic changes in a series of nine patients characterized clinically by hemiparesis, seizures, facial-asymmetry, and mental retardation[1]. The plain skull radiographic changes included thickening of calvarium and dilatation of ipsilateral frontal and ethmoid sinuses. Also, there was elevation of the greater wing of sphenoid and petrous ridge elevation of the greater wing of sphenoid and petrous ridge and upward tilting of planum- sphenoidale.

In 1939, Alpers and Dear defined two types of cerebral hemiatrophy[2]. In the primary (congenital) type, the entire cerebral hemisphere is characteristically hypoplastic. The secondary type results from a cerebrovascular lesion, inflammatory process, or cranial trauma. Twenty-two cases of primary variety were collected from the literature until 1939. A clinical triad of hemiplegia, seizures and mental retardation was defined. However mental retardation was not always present and seizures may appear months or years after the onset of hemiparesis[3].

According to Hageman et al, since primary cerebral atrophy is actually a lack of cerebral development rather than atrophy the term cerebral hemi-hypoplasia or unilateral cerebral hypoplasia would be more appropriate[4]. The brain reaches half of its adult size during the first year of life and reaches three-fourths of that size by the end of third year. As it enlarges, the brain presses outward on the bony tables and is partly responsible for the gradual enlargement and general shape of the adult head. When the brain fails to grow properly, the other structures tend to direct their growth inward, thus accounting for the enlargement of the frontal sinus, the increased width of the diploic space and the elevations of the greater wing of sphenoid and the petrous ridge on the affected side[5]. These changes can occur only when brain damage is sustained before three years of age however, such changes may become evident as soon as nine-months after brain damage was sustained[6].

A vascular cause of cerebral hemiatrophy (hypoplasia), first proposed in 1860 was confirmed in later studies[7,8,9]. It was proposed that a vascular anomaly occurring in very early gestation (five or six weeks) may result in a major defect in brain development whereas those occurring later may produce more localized lesions[8]. It was reported that decrease in carotid artery flow due to coarctation of aorta can also cause cerebral hemiatrophy. Crossed cerebellar atrophy is usually associated with long standing, extensive and unilateral cerebral lesions with onset during infancy or early childhood. The manifestations of DDMS may be so subtle as to be overlooked on plain radiographs; however, CT is the diagnostic modality of choice[8,9].

Both sexes and any of the hemispheres may be affected but male gender and left hemisphere involvement are more frequent. Age of presentation depends on time of neurologic insult and characteristic changes may be seen only in adolescence. The clinical findings may be of variable degree depending on the extent of the brain injury. Varying degrees of atrophy of one half of body, sensory loss, speech and language disorder, mental retardation or learning disability and psychiatric manifestations like schizophrenia may also be present.

A proper history, thorough clinical examination and radiologic findings provide the correct diagnosis. The condition needs to be differentiated from Basal ganglia

germinoma, Sturge Weber syndrome, Linear nervous syndrome, Fishman syndrome, Silver-Russell syndrome and Rasmussen encephalitis[5,6.]

A possible etiological relation between cerebral atrophy and seizures has been reported in two different studies from India[10,11,12,13.] Prognosis is better if hemiparesis occurs after the age of 2 yrs and in absence of prolonged or recurrent seizures. Children with intractable disabling seizures and hemiplegia are the potential candidates for hemispherectomy with a success rate of 85% in carefully selected cases.

Conclusion:

Although Dyke- Davidoff-Masson syndrome is a rare condition, its typical radiological findings can derive its diagnosis in the background of appropriate clinical features.

References:

1. **Dyke C G, Davidoff L M and Masson C B.** Cerebral Hemiatrophy and homolateral hypertrophy of the skull and sinuses. Surg Gynecol Obstet 1933; 57: 588-600.

2. **Alpers B J and Dear R B**. Hemiatrophy of the brain. J Nerv Ment Dis 1939; 89: 653-651.

3. **Zilkha A**. CT of cerebral hemiatrophy, AJR 1980; 135: 259-262.

4. **Hageman G, Gooskens R H J M, Willemse J, A**. cerebral cause of arthrogryposis: Unilateral cerebral hypoplasia. Clin Neurol Neurosurg 1985; 87: 119-119-122.

5. **Parker C E, Harris N, Mavalwala J.** Dyke-Davidoff-Masson Syndrome: Five case studies and deductions from dermatoglyphics. Clinical Pediatrics, 1972; 11(5): 288-292.

6. **Solomon G E, Hilal S K, Gold A P, et al.** Natural history of acute hemiplegia of childhood. Brain 1970; 93: 107-120.

7. **Teal J S, Rumbaugh C L, Bergeron R T, et al.** Congenital absence of internal carotid artery associated with cerebral hemiatrophy, absence of the external carotid artery. AJR 1973; 18: 534-545.

8. **Parker J C, Gaede J T**. Occurrence of vascular anomalies in unilateral cerebral hypoplasia "cerebral hemiatrophy". Arch Pathol Lab Med 1970; 90: 265-270.

9. **Tasdemir HA, Incesu L, Yazicioglu AK, Belet U, Gungor L**. Dyke Davidoff Masson syndrome. Clin Imaging 2002; 26: 13-17.

10. **Sharma S, Goyal D, Negi A, Sood RG, Jhobta A, Surya M**. Dyke-Davidoff Masson syndrome. Indian J Radiol Imaging 2006;16:165-166.

11. **Rao KCVG**. Degenerative diseases and hydrocephalus. In: Lee SH, Rao KCVG, Zimmerman RA, editors. Cranial MRI and CT. Fourth edition. New York: McGraw-Hill; 1999. p. 212-214.

12. **Nair KP, Jayakumar PN, Taly AB, Arunodaya GR, Swamy HS, Shanmugam V**. CT in simple partial seizures in children: a clinical and computed tomography study. Acta Neurol Scand 1997; 95: 197-200.

13. **Garg RK, Karak B**. Cerebral hemiatrophy: a possible etiological relation with febrile seizures. Indian Pediatr 1998; 35: 79

Correspondence Address: Dr.*Naba Raj Koirala,* Professor and Head, Department of Psychiatry and Mental Health, Nobel Medical College and Teaching Hospital, Biratnagar. E-mail: drnabaraj@yahoo.com.