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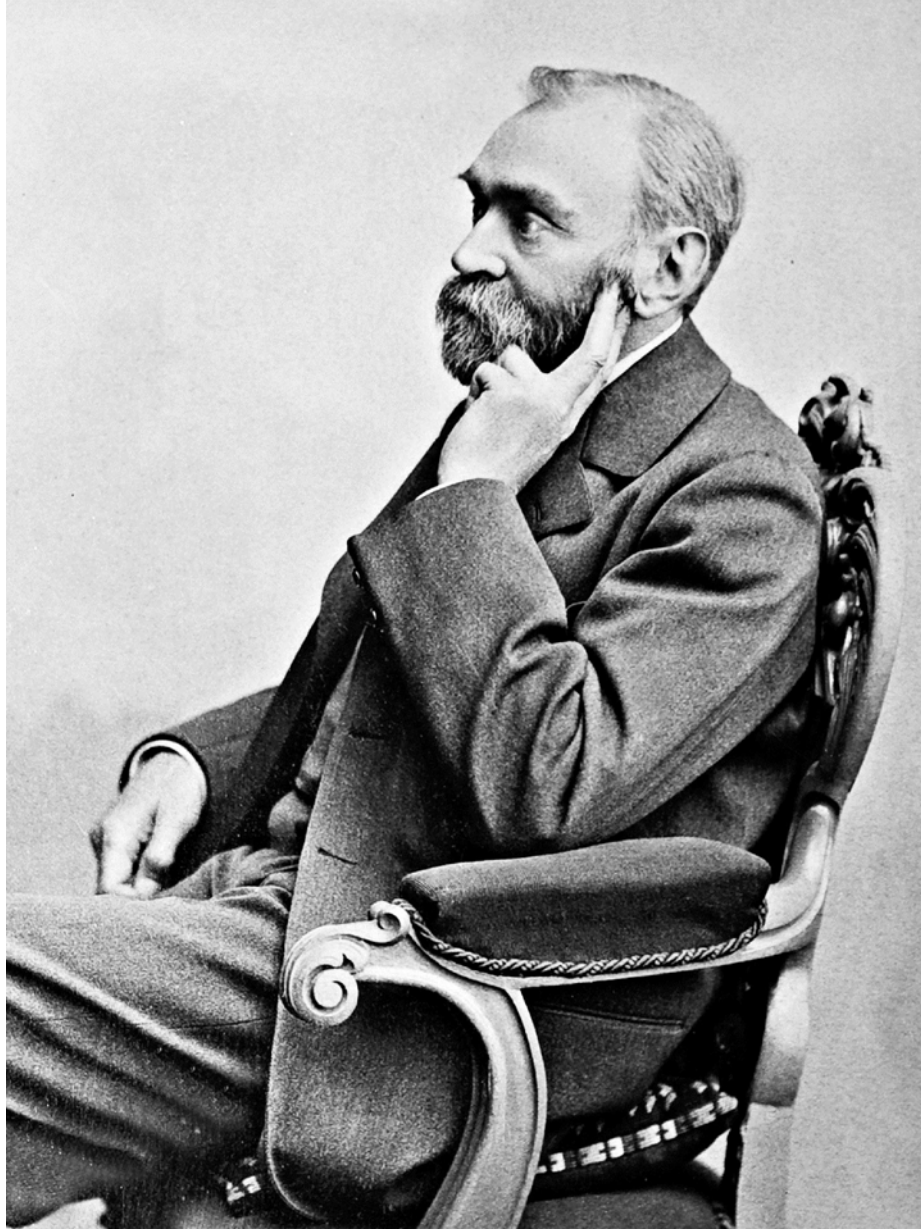
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ALFRED BERNHARD NOBEL

Alfred Bernhard Nobel was a Swedish chemist, engineer, innovator, and armaments manufacturer. He was the inventor of dynamite.

Born: October 21, 1833, Stockholm **Died:** December 10, 1896, Sanremo

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Editorial

God, The Creator Versus Man, The Explorer and Manipulator

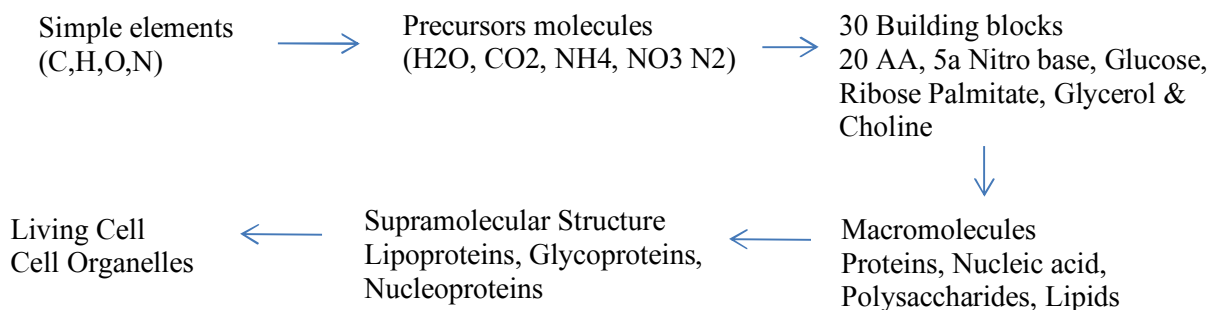
Dear faculty members

Greetings,

The content of this editorial under the heading 'God, the creator versus man, the explorer and manipulator is a creation of imagination with an intension of supporting the idea of existence of a superpower, the God as the creator of every living system including mankind and man, as explorers. All the research works carrying out by man will be taken as the exploration of the secretes already created by God.

Now, let us insert as short definition of life and the death in a language of chemistry. **"Life is a functionally organized state of elements and molecules. Disease and ultimately death is a state of disorder of these components."** This very definition itself supports the fact that any living body on this earth is made up of elements and molecules available on this earth. Again if we are to accept the theory of special creation already supported by three big groups; **Christians Muslims, and Jews**, we have to accept God, the almighty, as the creator. After repeated analysis of samples of human body, we have come to know that 6 elements i.e. carbon, hydrogen, oxygen, nitrogen, phosphorus and sulfur are the elements contributing 90% mass in the making of human body. Dust particles, God has collected from the surface of the earth for the creation of the first man as claimed by the Christians, could be a mixture of complex molecules consisting of those 6 elements along with other elements required in smaller quantities. Another information we have been getting from the books is that molecules are lifeless yet, in appropriate complexity and number, a living system comes into existence.

God, being a super-power, might be knowing all the techniques for construction of complex molecules, by organification of inorganic components through His divine power. Compromising with the findings of the analysis report of living bodies, we can imagine the possible steps of creation of life by God as outlined below.



The first set of living species including mankind, created by God, will be taken as standard, all systems being fixed correctly to their respective positions. Because of any mistake committed by mankind, if the systems are altered, the effect will be depicted in the form of diseases. Under such conditions, man, being the most intelligent living species created by God, start thinking for the exploration of the defective sites for correction. This is how man started researching of everything including human system. One major hurdle facing by man is the exploration and correction of disease processes caused by the alteration in the genetic

systems. For most of such cases, their efforts always remain at a stage yet to be completed. However, human interest for their exploration in this field is still increasing. For many of the complicated project works, ethical clearance is to be taken from the highest body. On the other hand, for some projects, seeing the importance of the work, the Government itself comes out for help.

Very recently, we came across one such project where man's manipulation skill being aimed at using for a good cause. We are taking the advantage of submitting a summary of this topic as a part of this editorial. We know this may not be a surprise for our colleagues in the department of Obs/Gynae. As mention above, simply we want to insert this as a message of human skill in manipulating God's created system for the sake of saving children in a family, already fixed for dying untimely generation after generations.

"Three- parent's in vitro fertilization, Gene replacement for the prevention of inherited mitochondrial disease." is the name of the topic.

It is a known fact that during conception, the fertilized egg has nuclear DNA from both the parents (99% DNA) with almost all the genes responsible for all the traits. However, the egg inherits the exact copy of the mitochondrial DNA (mt DNA) only from the mother. If the mother's mt DNA is defective, it can cause severe or deadly disease in the baby. If we can remove mother's faulty mt DNA and replace it by a healthy one from a donor? That's exactly what 3 -Parents IVF will be doing.

Two of the widely accepted techniques are as detailed below:

Pronuclear transfer technique: (i) Mother's egg with defective mitochondria DNA fertilized by father's sperm (ii) From a donor's fertilized egg with healthy mitochondrial DNA, the nucleus extracted and discarded to get enucleated egg (iii) The nucleus from fertilized mother's egg extracted and transferred to the enucleated donor's egg discarding the rest with the defective mitochondrial DNA (iv) The reconstituted fertilized egg transferred to the mother's womb.

Maternal spindle transfer technique (A micromanipulation technique):- (i) The nucleus or the spindle of chromosome removed from the unfertilized mother's egg with defective mitochondrial DNA and the rest discarded (ii) The nucleus of female donor's egg with healthy mitochondrial DNA also removed and discarded leaving the egg with healthy mitochondrial DNA (iii) The nucleus of the mother inserted into the enucleated donor's egg and fertilized by father's sperm (iv) The reconstituted egg transferred to the mother's womb.

Now UK is the first country to approve the procedure and the first country to approve law to allow the creation of babies from three people. The reason why we are submitting this topic for your disposal is because of the following facts. (i)The child will be inheriting the whole set of mitochondria from the 3rd parent (neither from the father nor from mother)(ii) Almost 1% of the baby's genetic material will also be inherited from the same donor (non from the parents) (iii) This set of mitochondria and mt DNA will be passing on to the next generation of the family (non from the parents) (iv) Thirteen very important proteins in the form of enzymes will be generated from that donated DNA (v) Major amount of ATP requirement of the child will be from that mitochondrial system run by those generated enzymes (vi) If the parents still want their own child without the donor, the result will be a child to be suffered his or her whole life due to the lack of sufficient ATP supply.

Now, the option is yours. One option is still left that is adoption of a genetically unrelated child. So, friends, if you come across any such condition in any of the families and if they don't want or cannot afford going for the above mention technique, kindly adopt a child who is really helpless instead of trying to get their own child. He/she will become countable assets for their rest of their lives.

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Original Article

Phenotypic study of Macrolide-Lincosamide-Streptogramin B Resistance in *Staphylococcus aureus* and their relationship with Methicillin-Resistant *Staphylococcus aureus* (MRSA) at Tertiary Care in Eastern Nepal

***Ganesh Kumar Singh, Bigu Kumar Chaudhari, Kamal Prasad Parajuli,**

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Abstract**Background**

Resistance to antimicrobial agents is prevalent among *Staphylococci*. This has led to wide uses of macrolide-lincosamide-streptogramin B (MLS_B) antibiotics to treat *Staphylococcus aureus* (*S. aureus*) infections. MLS_B though chemically distinct, have similar target site and mode of action. The multiple mechanisms are responsible for resistance to MLS_B antibiotics which can lead to clinical failure. The aim of the study was to investigate the frequency of inducible and constitutive clindamycin resistance among clinical isolates of *S. aureus* and their relationship with Methicillin-resistant *Staphylococcus aureus* (MRSA).

Material & Methods

A total of 336 unique *Staphylococcus aureus* isolates from different clinical samples obtained from patients were studied. Antibiotic susceptibility test was performed by Kirby-Bauer disc diffusion method. "D test" was performed to detect inducible clindamycin resistance as per CLSI guidelines. MRSA was detected using Cefoxitin (30µg) and results were interpreted according to CLSI criteria.

Results

Inducible clindamycin resistance was seen in 45 (13.39%), constitutive clindamycin resistance was seen among 58 (17.26%) while MS phenotype was observed among 38(11.30%) of isolates. Inducible resistance as well as constitutive resistance was higher among MRSA as compared to MSSA (21.11%, 4.48% and 21.11%, 12.82% respectively).

Conclusion

The Successful use of clindamycin for the treatment of infection caused by *S. aureus* can be predicted based on the result of simple and inexpensive D test.

Key Words: *Clindamycin resistance, iMLS_B, MRSA, Nepal*

Introduction

Staphylococcus aureus (*S. aureus*) is one of the most frequent microorganisms responsible for both community and hospital acquired infections. Methicillin resistance *Staphylococcus aureus* (MRSA)

which are resistance to multiple classes of antibiotics often pose problems in therapy. This has renewed concern for the usage of Macrolide-Lincosamide-Streptogramin B (MLS_B) antibiotics to treat *S. aureus* infections [1]. Clindamycin, a lincosamide,

is a preferred option to treat infections, especially skin and soft tissue caused by both methicillin resistant and methicillin susceptible *S. aureus* because of the various reasons [2]. However, because of extensive use of MLS_B antibiotics high incidence MLS_B resistant Staphylococcal strains are reported [3, 4]. The resistance to macrolide is either due to active efflux of antibiotics mediated by protein encoded by *msrA* gene or due to modification of ribosome by r-RNA methylase enzymes encoded by *erm* genes which confer inducible or constitutive resistance to MLS_B antibiotics. In constitutive resistance (cMLS_B), the enzyme r-RNA methylase is constitutively produced while in inducible resistance (iMLS_B) it is produced only in the presence of inducible agent [5]. Low level erythromycin is the most efficient inducer of iMLS_B resistance. *In vitro*, constitutively resistance *Staphylococcus aureus* are resistant to both erythromycin and clindamycin whereas those with inducible resistance are resistant to erythromycin and appear sensitive to clindamycin [6]. If clindamycin is used to treat patients harbouring iMLS_B *Staphylococcus*, selection for constitutive *erm* mutants occur leading to therapeutic failure [7]. The objective of the present study was to investigate the prevalence of inducible clindamycin resistance among *Staphylococcus aureus* isolated from our teaching hospital and to detect their distribution among Methicillin-resistant *Staphylococcus aureus* (MRSA).

Material and Methods

This study was a prospective study conducted from 1st January 2015 to 30th June 2015. A total of 336 non-duplicate *Staphylococcus aureus* isolates from different clinical samples obtained from patients attending Nobel Medical College and Teaching Hospital, Biratnagar, Nepal were studied. The isolates were identified as *Staphylococcus aureus* using standard microbiological procedures [8].

Antimicrobial susceptibility testing was done by Kirby-Bauer's disc diffusion method on Muller Hinton agar using various antimicrobial agents: penicillin (5µg), cefoxitin (30µg), amikacin (30µg), erythromycin (15µg), cotrimoxazole (1.25/23.75µg), chloramphenicol (30µg), clindamycin (2µg), teicoplanin (30µg), linezolid (30µg) as per CLSI guidelines [9].

MRSA was detected by Kirby Bauer disc diffusion method using 30µg cefoxitin disc on Muller Hinton Agar seeded with 0.5 McFarland bacterial suspensions. After overnight incubation at 35°C, the results were interpreted according to CLSI guidelines [9]. The strains were confirmed as Methicillin resistance by agar dilution method using Muller Hinton medium containing 4% NaCl and 6µg/mL oxacillin. *Staphylococcus aureus* NCTC 6571 and *S. aureus* NCTC 12493 were used as a control strain for methicillin-sensitive and methicillin-resistant strain respectively. Test to detect inducible clindamycin resistance was performed by placing erythromycin (15µg) disc and clindamycin (2µg) spaced 15mm from edge-to-edge on a Mueller-Hinton agar plate previously inoculated with 0.5 McFarland bacterial suspensions. Following overnight incubation at 35°C the results were read as per CLSI guidelines [9].

Three different phenotypes were observed after testing and were interpreted as follows:

1. MS Phenotype - Staphylococcal isolates resistance to erythromycin (zone size ≤13mm) and sensitive to clindamycin (zone size ≥21mm) giving circular zone of inhibition around clindamycin.

2. Inducible MLS_B (iMLS_B) Phenotype - Staphylococcal isolates resistance to erythromycin and sensitive to clindamycin with D - shaped zone of inhibition adjacent to erythromycin disc.

3. Constitutive MLS_B (cMLS_B) Phenotype - Staphylococcal isolates resistance to both

erythromycin and clindamycin (zone size ≤ 14 mm) with circular shape of zone of inhibition if any around clindamycin. *S. aureus* ATCC 25923 was used for routine quality control of the erythromycin and clindamycin discs. Also an in-house chosen *S. aureus* with confirmed positive and negative D-test were used as additional quality control.

Statistical analysis to study the relationship between MRSA and inducible clindamycin resistance was carried out using SPSS version 16.

Results

Out of the 336 *S. aureus* isolates tested, 180 (53.57%) strains were found to be MRSA. Results of D-test analysis showed that out of 336 *S. aureus* 45 (13.39%) were positive for D test. Constitutive clindamycin resistance was observed in 58 (17.26%) isolates [Table 1]. Prevalence of inducible as well as constitutive resistance was higher among MRSA as compared to MSSA (Chi-square test, $p < 0.001$) [Table 2]. All the isolates showing inducible clindamycin resistance were susceptible to chloramphenicol, linezolid, and teicoplanin [Table 3].

Table:1 Susceptibility pattern against Erythromycin and Clindamycin among total *S. aureus* isolates

Susceptibility pattern (Phenotype)	No. of isolates	Percentage
Sensitive to both erythromycin and clindamycin	195	58.03
Resistant to both erythromycin and clindamycin (cMLS _B)	58	17.26
Erythromycin resistant and clindamycin sensitive (D test positive, iMLS _B)	45	13.39
Erythromycin resistant and clindamycin sensitive (D test negative, MS)	38	11.30
Total	336	100

Discussion

Testing for antimicrobial susceptibility among the clinical isolates of microorganisms is crucial for the optimum outcome of the treatment. This is

particularly important as the number of resistance is increasing day by day.

Table:2 Susceptibility pattern against Erythromycin and Clindamycin among Methicillin Resistant *S. aureus*(MRSA) isolates

Isolate	E-S, CD-S	E-R, CD-R (cMLS _B)	E-R,CD-S, (D test positive, iMLS _B)	E-R, CD-S (D test negative, MS)
MRSA (180)	87 (48.33)	38 (21.11)	38 (21.11)	17 (9.44)
MSSA (156)	108 (69.23)	20 (12.82)	7 (4.48)	21 (13.46)
Total (336)	195 (58.03)	58 (17.26)	45 (13.39)	38 (11.30)

E = erythromycin, CD = clindamycin, S = sensitive, R = resistant, cMLS_B = constitutive MLS_B phenotype, iMLS_B = inducible MLS_B phenotype, MS = MS phenotype

Table:3 Susceptibility pattern of inducible resistant (iMLS_B) phenotype

Antimicrobial agents	No. of sensitive strain	No. of resistant strain
Methicillin	7	38
Penicillin	0	45
Amikacin	41	4
Chloramphenicol	45	0
Cotrimoxazole	32	13
Linezolid	45	0
Teicoplanin	45	0

Recently clindamycin has become an excellent drug for the treatment of infections especially skin and soft tissues infections caused by *Staphylococcus aureus* [6]. However, Staphylococcal isolates with inducible phenotypes develops resistance to clindamycin and from such phenotypes mutants with constitutive resistance can arise spontaneously during clindamycin therapy [10]. Therefore, Staphylococcal isolates must be checked for inducible resistance before they are reported as susceptible to clindamycin to prevent therapeutic failure because isolates that demonstrate negative result for inducible clindamycin resistance confirms susceptibility to clindamycin and provide better therapeutic option [11]. In our study overall prevalence of inducible clindamycin resistance (iMLS_B) among the *Staphylococcus aureus* was 13.39%. Such an occurrence is similar to that reported by Ansari *et al* (12.4%) and Sah *et al* (12.1%) from Nepal [12, 13]. In contrary this

finding was low as compared to other reports from Nepal and other part of the world [10, 14-18]. Constitutive resistance (cMLS_B) (17.26%) obtained in present study was low as compared another reports [10, 14-16]. Such variations could be because of differences in period of study, patient group and geographical locations.

The present study demonstrated higher prevalence of iMLS_B and cMLS_B among the MRSA as compared to MSSA. This finding is in concordance with other reports [13-16]. On the contrary, certain reports suggest a remarkably greater occurrence of iMLS_B among MSSA [19-21].

Clindamycin, by virtue of its excellent bone and tissue penetration and accumulation in abscesses, has become a useful antibiotic for the treatment of serious infections caused by methicillin sensitive as well as methicillin resistant *Staphylococcus aureus*. Further clindamycin is an alternative for penicillin-allergic patients. Better oral absorption and lack of need for renal adjustment makes it an important therapeutic agent [5]. However major risk with the use of clindamycin as a therapeutic agent is existence of iMLS_B and cMLS_B among *S. aureus* and its use for the treatment of patients harboring iMLS_B phenotype will lead to therapeutic failure. However there are reports which states that infections caused by *S. aureus* expressing iMLS_B resistance can successfully be treated with clindamycin [6]. Hence, limiting the use of clindamycin for the treatment of *S. aureus* is not desirable [22]. Therefore D test should be performed routinely and the clinician should be informed regarding the possible failure of clindamycin therapy in infections caused by *S. aureus* harboring iMLS_B resistance.

Conclusion

The high incidence of staphylococcal infections all over the world and emergence of multi drug resistance has led

use of clindamycin for the treatment of infections caused by *S. aureus* [15]. As clindamycin is not a drug of choice for D – test positive isolates while it can definitely be a suitable drug in D - test negative isolates, performance of D - test in a routine laboratory will enable us to guide the clinicians in judicious use of clindamycin.

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Original Article

Angiographic study of Coronary Artery Dominance in Nepalese Population

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Abstract

Background

The dominance of coronary artery in our population is not known. This study aims to identify dominant coronary artery in Nepalese population.

Material and Methods

This study was carried out in the Cath Lab of Manmohan cardiovascular and thoracic centre Kathmandu over a period of 18 months (August 2012 to April 2014). All patients of either gender who presented to the Cath lab for coronary angiography for different indications were included in the study. Patients with congenital heart diseases who were below the age of 18 years were excluded.

Results

A total of 667 patients were enrolled out of which 69% (n=488) were male and 31% (n=219) were female. The mean age was 51.3(30-76) years. Right coronary artery was dominant in 83%, left dominant in 10% and co-dominant in 7% of the patient population.

Conclusion

The right coronary dominant pattern is more prevalent in our population. Gender has no significant association with coronary dominance.

Key Words: *Coronary angiography, Dominant coronary artery, gender difference*

Introduction

Two main coronary arteries (left and right) arise from the ascending aorta. Left main coronary artery divides into left anterior descending (LAD) and left circumflex (LCx) artery. Right coronary artery divides into posterior descending artery (PDA) and posterolateral branches (PLBs). LAD supplies blood to the front of the left side of the heart. LCx supplies blood to the back and the lateral side of the heart. RCA supplies blood to the right atrium, right ventricle, SA node, AV node and variable portion of left ventricle [1].

Coronary artery dominance is classified as left dominance, right artery dominance, and co-dominant [2]. The dominant vessel supplies the posterior descending artery and at least one posterolateral branch. The RCA is dominant in 85% of patients. The RCA is non dominant in 15% of patients in which one half have PDA and posterolateral branch arising from the distal circumflex artery called left dominance and in the remaining half the RCA gives rise to PDA and the LCx provides all the posterolateral branches called co dominant circulation [1]. The pattern of dominant vessel varies in different populations. The

dominant pattern has clinical significance as the ECG changes and the region of involvement in ST segment elevation myocardial infarction is different. Knowledge of coronary artery variations and pathologies is important in planning the treatment and in interpretation of findings of cardiovascular diseases. This study aims to determine the pattern of coronary artery dominance in our population.

Material and Methods

This case series study was carried out in Cath Lab of Manmohan cardiovascular and thoracic centre Kathamandu over a period of 18 months. All patients of either gender over 18 years of age who presented to the Cath lab for coronary angiography for different indications were included in the study except those who had congenital heart diseases. The demographic profile of the patients and pattern of coronary artery dominance were recorded on a proforma. All standard views were taken during coronary angiography with special focus on left anterior oblique cranial view to document left dominant system. The data were analyzed through SPSS version 16. Various descriptive statistics were used to calculate frequencies, percentages and means values. Numerical data such as age were expressed as mean \pm standard deviation while the categorical data were expressed as frequency and percentages.

Results

A total of 667 patients underwent diagnostic CAG during the specified period. Two hundred and ninety (31%) were women and four hundred and eighty-eight (69%) were men.

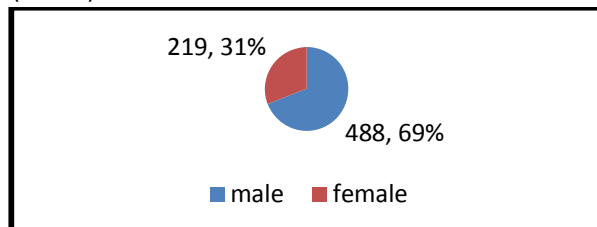


Fig 1. Gender distribution

The mean age was 51.3 years. Age range was 30-76 years. Right coronary artery was dominant in 83%,

left dominant in 10% and co-dominant in 7% of the patient population.

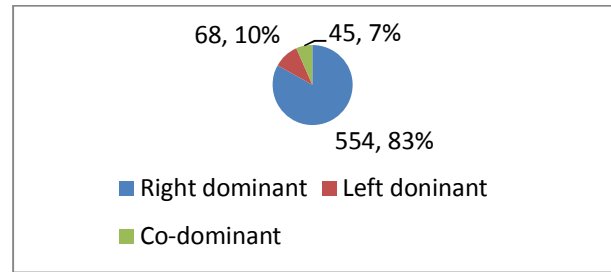


Fig 2 Coronary artery dominance

Among the right dominant group 416 were male and 138 were female. In the left dominant group 64 were male and 24 were female. In co-dominant group 28 were male and 17 were female.

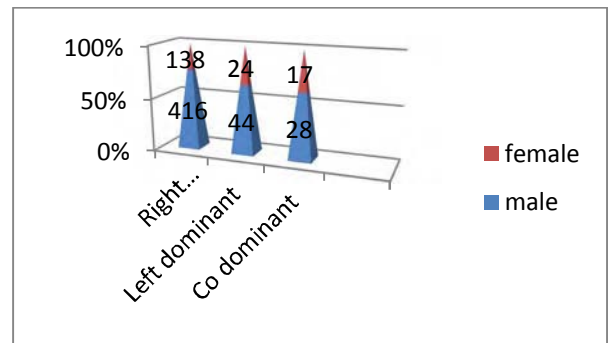


Fig 3. Gender wise distribution of coronary dominance

Discussion

In our study, 83% had RCA dominance, 10% had LCx dominance and 7% had co-dominant coronary circulation. There is no significant difference in dominance pattern with age or sex. The pattern of coronary artery dominance is different in different communities. In a study by Altaii et al, right dominance was found in 83%, left dominance in 14.5% and co dominance in 2.5% cases [3]. The prevalence of right dominance in studies reported from Kenya, Brazil, and Iran has also been same with the range 82% - 84.2% [4-6]. However, right dominance was significantly less common (60.5%) in a study from Pakistan [7]. Nearly 20% subjects each in this study had either a dominant LCX or a co-dominant pattern.

In all the studies right dominance was the most common type though the frequency differs in different study. Right dominant circulation was more prevalent in our study also. This finding is in conformity with what is reported in the published literature.

Limitations

This is study of single Centre with 667 patients. The numbers are small and only of one centre. Large number of patients with multicentre involvement is recommended to find out coronary artery dominance in Nepalese population. However as in other studies, this study also showed Right dominance is most common pattern of coronary dominance.

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Original Article

Intelligence Quotient Levels and Sub Tests Comparison in Autistic Children

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Abstract

Background

Autism spectrum disorders (ASD) are disorders of neurodevelopmental origin characterized by social reciprocity deficits, communication deficits, and unusual restricted and repetitive behaviors. In some of these people, measured IQ (Intelligence Quotient) can be normal or even superior or low.

Material and Methods

This is a Retrospective study in autistic children. We have analyzed with autistic disorder, 47 patients had savant skills and 1 patients of MR (Mental Retardation) had savant skills. China- Wechsler Young Children Scale of Intelligence (C-WYCSI) and China-Wechsler Intelligence Scale for Children(C-WISC) were used for calculating IQ levels in different age groups.

Results

Asperger's syndrome (AS) children had higher verbal IQ (VIQ) and full scale IQ (FSIQ) compared to autism and high functional autism (HFA) children with statistical difference. Autism children had lower VIQ, performance IQ and FSIQ compared to HFA and AS children with statistical significance. AS children had higher values in C-WISC and C-WYCSI compared to autism children.

Conclusion

Children with Asperger's syndrome have higher full IQ and Sub test IQ compared with autism and HFA children.

Key Words: *Autism, Asperger's syndrome, IQ (Intelligence Quotient) level, high functional autism, mental retardation*

Introduction

Autism spectrum disorders (ASD) are disorders of neurodevelopmental origin characterized by social reciprocity deficits, communication deficits, and unusual restricted and repetitive behaviors. [1-2]. Aside dysfunctions in the behavior, individuals with autism may present multiple undefined or even prominent cognitive functions [3]. In some of these autistic individuals, normal or low and even

superior measured IQ is a possibility. Thus as in savant syndrome, low IQ score is not the required case in all instances.

Material and Methods

This is a retrospective study of autistic children. Patients visiting the out patients department of Child Developmental and Behavioral Division, Nobel Medical College Teaching Hospital Biratnagar, Nepal were enrolled in this study from August 09,

2011 to May 08, 2014. Forty eight cases were enrolled in the study, out of which 47 patients with autistic disorder and 1 patient of MR. Of these 48 children; there were 45 male, and 3 female with mean and SD of age 7.08 ± 2.31 years. Number of Autistic disorders in children group includes 11 Autism, 10 high functional autism (HFA), and 26 Asperger's syndrome (AS), 1 mental retardation (MR). Children with less than two and half years old and those without IQ report were not included in this study.

China- Wechsler Young Children Scale of Intelligence (C-WYCSI) and China-Wechsler Intelligence Scale for Children (C-WISC) were used for calculating IQ levels in different age groups. C-WYCSI was used as a test for calculating IQ in children between 4 years and 6 years 6 months. The C-WYCSI is a colorful, current, and interesting IQ test for children. It measures Full Scale IQ, Verbal IQ, Performance IQ, and Processing Speed and has an optional General Language Composite. IQ stands for Intelligent Quotient. It indicates a person's intelligence by an intelligence test. The C-WYCSI is composed of 11 subtests: Knowledge, Picture Naming, Arithmetic, Picture summarizing, Comprehension, Animals lay eggs, Picture Completion, Maze, Visual analysis, Block design, Geometry diagram. C-WISC was used as a test for age range between 6 years and 16 years 11 months.

The C-WISC is a test that does not require reading or writing for individual testing. Oral questions are asked in the verbal subtests with no time limits except for mathematical problems. Nonverbal problems make up the performance subtests, all of which have time limits and bonus points are allowed in some of them for rapid work. Older students requiring speed bonuses to obtain better-than-average scores are the criticizing part of C-WISC-III. The C-WISC is composed of 11

subtests: Information, Similarities, Arithmetic, Vocabulary, Comprehension, Digit span, Picture completion, Picture arrangement, Block design, Object assembly, Coding. Verbal IQ (VIQ), Performance (nonverbal) IQ (PIQ), Full Scale IQ (FSIQ), subtests and IQ percentile rank analysis.

SPSS 16.0 (SPSS Inc., Chicago, IL) was used during the analysis. ANOVA (analysis of variance) and Post Hoc analysis (LSD) was done to find out the difference in various C-WISC, C-WYCSI parameters and IQ difference in autistic children. All the variables are expressed as mean \pm standard deviation. Any case with $p < 0.05$ was considered to be significant.

Results

We compared 3 elements between Autism, HFA and AS. ANOVA (analysis of variance) and Post Hoc analysis (LSD) was done.

Verbal IQ (VIQ) was significant between Autism and HFA (57.6 ± 13.1 vs 75.9 ± 12.1 , $p = 0.010$), highly significant between Autism and AS (57.6 ± 13.1 vs 102.7 ± 17.5 , $p = 0.000$) and highly significant between HFA and AS (75.9 ± 12.1 vs 102.7 ± 17.5 , $p = 0.000$). Performance IQ (PIQ) was significant between Autism and HFA (62.4 ± 14.3 vs 85.7 ± 19.1 , $p = 0.001$) and highly significant between Autism and AS (62.4 ± 14.3 vs 96.3 ± 14.8 , $p = 0.000$). Full Scale IQ (FSIQ) was significant between Autism and HFA (55.4 ± 11.8 vs 78.7 ± 8.4 , $p = 0.000$), significant between Autism and AS (55.4 ± 11.8 vs 99.7 ± 13.7 , $p = 0.000$) and significant between HFA and AS (78.7 ± 8.4 vs 99.7 ± 13.7 , $p = 0.000$). Result showed that AS children had higher VIQ and FSIQ compared to autism and HFA children with statistical significant difference. Autism children had lower VIQ, PIQ and FSIQ compared to HFA and AS children with statistical significance as shown in table 1.

Table 1: VIQ, PIQ and FSIQ in different children group

	Mean and standard deviation for			p * _{va} lue	p ** val ue	p *** _v alue
	Autism n=11	HFA n=10	AS n=26			
VIQ	57.6±13.1	75.9±12.1	102.7±17.5	0.010	0.000	0.000
PIQ	62.4±14.3	85.7±19.1	96.3±14.8	0.001	0.000	0.076
FSIQ	55.4±11.8	78.7±8.4	99.7±13.7	0.000	0.000	0.000

*P** = Autism vs HFA, *p*** Autism vs AS, *p**** HFA vs AS

We compared 11 subtests of C-WISC between Autism, HFA and AS children. ANOVA and Post Hoc analysis (LSD) was done. Information subtest was significant between Autism and AS (5.2 ± 3.7 vs 14.5 ± 6.3 , $p = 0.000$) and it was also significant between HFA and AS (8.8 ± 3.7 vs 14.5 ± 6.3 , $p = 0.048$). Similarities subtest was significant only between Autism and AS (15.2 ± 12.2 vs 34.0 ± 5.2 , $p = 0.000$).

Arithmetic subtest was significant only between Autism and AS (5.5 ± 4.1 vs 13.9 ± 4.8 , $p = 0.000$). Vocabulary subtest was significant only between Autism and AS (4.2 ± 5.0 vs 12.6 ± 7.7 , $p = 0.006$). Comprehension subtest was significant between Autism and AS (4.5 ± 5.1 vs 12.9 ± 4.0 , $p = 0.000$) and significant between HFA and AS (7.4 ± 4.2 vs 12.9 ± 4.0 , $p = 0.010$). Picture completion was significant between Autism and AS (3.0 ± 2.8 vs 6.0 ± 2.5 , $p = 0.016$). Picture arrangement was highly significant between Autism and AS (1.8 ± 1.4 vs 12.8 ± 6.9 , $p = 0.000$) and significant between HFA and AS (4.6 ± 3.6 vs 12.8 ± 6.9 , $p = 0.007$). Block design was significant between Autism and AS (10.2 ± 8.9 vs 23.9 ± 13.4 , $p = 0.008$) and significant between HFA and AS (11.0 ± 4.0 vs 23.9 ± 13.4 , $p = 0.033$).

Object assessment was significant only between Autism and AS (4.2 ± 2.2 vs 17.2 ± 10.6 , $p = 0.002$). Coding was significant between Autism and AS (18.9 ± 9.1 vs 40.3 ± 16.7 , $p = 0.001$) and significant between HFA and AS (25.0 ± 3.2 vs 40.3 ± 16.7 , $p = 0.037$) as shown in table 2.

Table 2: C-WISC between autism, HFA and AS children

	Mean and std. deviation for			p * _v alu e	p *** _v alue	p *** valu e
	Autism n=8	HFA n=5	AS n=19			
Information	5.2±3.7	8.8±3.7	14.5±6.3	0.263	0.000	0.048
Similarities	15.2±12.2	25.2±13.6	34.0±5.2	0.058	0.000	0.058
Arithmetic	5.5±4.1	9.4±5.0	13.9±4.8	0.154	0.000	0.066
Vocabulary	4.2±5.0	6.6±4.4	12.6±7.7	0.544	0.006	0.085
Comprehension	4.5±5.1	7.4±4.2	12.9±4.0	0.216	0.000	0.010
Digit span	9.4±2.8	9.0±3.2	11.5±2.7	0.816	0.079	0.084
Picture completion	3.0±2.8	4.4±3.9	6.0±2.5	0.385	0.016	0.263
Picture arrangement	1.8±1.4	4.6±3.6	12.8±6.9	0.385	0.000	0.007
Block design	10.2±8.9	11.0±4.0	23.9±13.4	0.910	0.008	0.033
Object assessment	4.2±2.2	9.6±10.0	17.2±10.6	0.316	0.002	0.110
Coding	18.9±9.1	25.0±3.2	40.3±16.7	0.447	0.001	0.037

*P** = Autism vs HFA, *p*** Autism vs AS, *p**** HFA vs AS

Result showed that there was difference in various C-WISC parameters between AS children in comparison to Autism and HFA children.

We compared 11 subtests of C-WYCSI between Autism, HFA and AS children. ANOVA and Post Hoc analysis (LSD) was done. Knowledge subtest was significant only between Autism and AS (3.3 ± 1.5 vs 10.3 ± 4.6 , $p=0.019$). Picture naming subtest was significant between Autism and HFA (11.0 ± 10.1 vs 23.6 ± 3.2 , $p=0.020$) and significant between Autism and AS (11.0 ± 10.1 vs 29.4 ± 6.5 , $p=0.001$). Arithmetic subtest was significant between Autism and AS (7.0 ± 6.6 vs 13.4 ± 2.8 , $p=0.032$) and significant between HFA and AS (8.2 ± 3.3 vs 13.4 ± 2.8 , $p=0.038$). Picture summary was significant only between Autism and AS (18.0 ± 16.7 vs 44.1 ± 16.1 , $p=0.021$). Comprehension subtest was significant only between Autism and AS (3.0 ± 5.2 vs 11.7 ± 5.5 , $p=0.032$) as shown in table 3.

Table 3: C-WYCSI between Autism, HFA and AS children

	Mean and std. deviation for			p_{*v} Alu e	p_{**v} Alu e	p_{***} value
	Autism n=3	HFA n=5	AS n=7			
Knowledge	3.3 ± 1.5	7.0 ± 2.8	10.3 ± 4.6	0.202	0.019	0.157
Picture naming	11.0 ± 10.1	23.6 ± 3.2	29.4 ± 6.5	0.020	0.001	0.149
Arithmetic	7.0 ± 6.6	8.2 ± 3.3	13.4 ± 2.8	0.066	0.032	0.038
Picture summary	18.0 ± 16.7	31.0 ± 9.3	44.1 ± 16.1	0.023	0.007	0.143
Comprehension	3.0 ± 5.2	5.6 ± 4.7	11.7 ± 5.5	0.050	0.032	0.068
Animal lay eggs	43.7 ± 28.2	60.2 ± 12.1	56.4 ± 19.3	0.026	0.054	0.743

Picture completion	4.7 ± 4.5	10.2 ± 5.8	10.0 ± 5.4	0.186	0.178	0.951
Maze	9.7 ± 11.9	15.0 ± 10.2	20.4 ± 10.8	0.051	0.174	0.407
Visual analysis	22.0 ± 5.2	27.6 ± 8.1	31.4 ± 5.4	0.025	0.054	0.327
Block design	2.7 ± 4.6	13.6 ± 10.9	13.4 ± 6.5	0.008	0.076	0.971
Geometric diagram	4.7 ± 5.0	8.6 ± 8.3	12.8 ± 9.0	0.052	0.175	0.394

$p^* = \text{Autism vs HFA}$, $p^{**} = \text{Autism vs AS}$, $p^{***} = \text{HFA vs AS}$

Result showed that there was difference in various C-WYSCI parameters between AS children in comparison to Autism children. AS children had higher C-WYSCI values in comparison to autism children and there was statistical significant difference seen in knowledge, picture naming, arithmetic, picture summary and comprehension parameters.

Discussion

During our study AS children have higher VIQ, FSIQ compared with Autism and HFA children with statistical significance. Asperger (1944/1991) has spoken of autistic intelligence as a true creative intelligence, adding for success in science or art [4]. And, Fitzgerald (2004), spoke of a number of intellectual prodigies having autistic traits [2] embracing the fact that a person with extraordinary skills might fall within the challenges autistic spectrum. When applied to autistic child, the term ‘mental disability’ can include disorders as Autism, High Functional Autism (HFA), Asperger’s Syndrome (AS). In some of the autistic individuals, normal or low and even superior measured IQ is a possibility. Thus a low IQ score is not the required case in all instances. Some autistic individuals score in the ordinary or extraordinary range on mostly used IQ tests, or at least on few

sub-tests that constitute the overall IQ test battery [5-8].

In our study, there was difference in various C-WISC parameters between AS children in comparison to autism and HFA children. AS children had higher values compared to autism children and statistical difference with $p < 0.05$ was seen in all parameters except digit span. In our study, there was difference in various C-WYSCI parameters between AS children in comparison to Autism children. AS children had higher C-WYSCI values in comparison to autism children and there was statistical significant difference seen in knowledge, picture naming, arithmetic, picture summary and comprehension parameters.

Limitations

1. This study has comparatively small sample size. This can lead to some bias during the analysis. A large scale study may be needed for investigating further.

2. We only had few investigations while comparing these children. It may be more helpful to find out the changes in the brain of these children and to justify the reasons for higher full scale IQ and sub IQ test, savant skills in AS children if CT, f-MRI etc. were done.

Conclusions

Children with Asperger's syndrome have higher full IQ and Sub test IQ compared with autism and HFA children.

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Original Article

Evaluation of prostate specific antigen level in different age group of Patients in Eastern part of Nepal

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Abstract

Background

A study was conducted to evaluate Prostate specific antigen (PSA) level in different age group of patients in Nobel Medical College Teaching Hospital (NMCTH), Biratnagar, Eastern Nepal.

Material and Methods

A total of 1870 male patients (age 51-88), attending OPD in different departments of NMCTH, were sent to Clinical Laboratory Services for estimation of Prostate specific antigen from 1st January 2013 to 30th June 2014 and recruited for this study after Institutional ethical approval.

Blood serum of these patients was tested for Prostate specific antigen level by Chemiluminescence Immunoassay (CLIA). Mean value and standard deviation were calculated using Student's two-tailed t-test. Analysis of data was performed using one-way ANOVA. Results are considered statistically significant if $p \leq 0.05$.

Results

Out of 1870 patients, 178 patients showed significantly higher level of PSA in their serum when compared to normal individuals. Out of this 178, 37 were from age group of 51-60, 51 were from age group of 61-70, 42 were from age group of 71-80 and 48 were from age group of 81-88. The remaining 1692 patients were having PSA within normal limit. PSA was found to be elevated up to a maximum of 34.5 ng/ml in patient. PSA level of <4 ng/ml was considered normal for this study.

Conclusion

This study, thus determines the diagnostic level of PSA, in different age group of patients comparing with normal individuals in eastern Part of Nepal that can help in diagnosis, prognosis and management of prostate cancer.

Key words: *CLIA, Eastern Nepal, Prostate cancer, PSA*

Introduction

The prostate specific Antigen (PSA) has been widely used to screen men for prostate cancer and it is the most common cancers afflicting men today. PSA level has got prognostic value too in diagnosed patients. PSA is accurate and precise

noninvasive biomarker and its diagnostic significance is well documented. One of the most common causes of death in men is Prostate cancer and it is the second most common cancer worldwide in males. Several factors like older age, ethnicity, family history and genetic and

environmental factors are the causes of the disease [1,2]. A serine protease enzyme, i. e. PSA having the mol. weight 33 kDa, is a set marker for screening, diagnosis and management of prostate cancer [3,4].

In Asian countries, the incidence of Prostate cancer (PCa) has been increasing in recent years, but until date it is still much lower than in Western countries.

PSA testing has been widely used for more than two decades to detect early PCa. However, its specificity is low, especially in the PSA "grayzone" (PSA 2.5–10.0 ng/ml) [5], while the mortality of PCa has greatly declined in many developed countries, it is increasing in less developed regions worldwide during the recent decade [6]. Genetic susceptibility has been indicated as a vital risk factor for PCa.

Techniques like transrectal ultrasound, biopsies, serum PSA and digital rectal examination are the tools used for early detection. The most reliable technique is PSA. In other conditions such as benign prostate hyperplasia and prostatitis, PSA can also be elevated.

In this present study, an attempt is made to screen suspected cases of PCa among people in the eastern part of Nepal by collecting those who are coming to the NMCTH OPD for a duration of one and half year by using PSA as marker. We have given the data of normal as well as elevated value of Prostate specific antigen (PSA) in different age group of patients.

Material and Methods

It is a hospital based study carried out in the Department of Biochemistry of the Nobel Medical College Teaching Hospital, Biratnagar, Nepal from 1st January 2013 to 30th June 2014 and recruited for this study after Institutional ethical approval.

A total of 1870 patients (age 51-88) from various department of NMCTH OPD were sent to Clinical Laboratory Services for estimation of PSA level. Blood Serum from these patients was tested for PSA level by

Chemiluminescence Immunoassay (CLIA). The standard procedure was followed as per manufacturer's instructions for CLIA (Aculite). Approval for the study was obtained from the institutional research committee and informed consent from the patients.

Inclusion criteria for the study

The male patients of age above 50 years have been included for this study.

Exclusion criteria for the study

The male patients of age less than 50 years have been excluded for this study.

Statistical Analysis

The data on PSA levels were analyzed using nonparametric kruskal-walli's one-way analysis of variance by ranks. Mean value and standard deviation were calculated using Student's two-tailed t-test. Analysis of data was performed using a student T-test or one-way ANOVA. Results are considered statistically significant if $p \leq 0.05$.

Results

Out of 1870 patients, age range of 51 years and 88 years, screened for PSA level by CLIA, 37 patients from age group of 51-60, 51 patients from age group of 61-70, 42 patients from age group of 71-80 and 48 patients from age group of 81-88 had significantly higher level of PSA and 1692 patients were having PSA within normal limit.

The PSA level was significantly elevated in all age group of patients of this study as compared to PSA range within normal limit [$p = 0.001$ for age group of 81-88, $p = 0.005$ for age group of 71-80, $p = 0.02$ for age group of 61-70, $p = 0.01$ for age group of 51-60, shown in Fig. 1].

From among the patients of 51-60 year age group, 37 patients had elevated level of PSA in which the highest and the lowest level of PSA of this group were 22.4ng/ml and 8.6 ng/ml respectively.

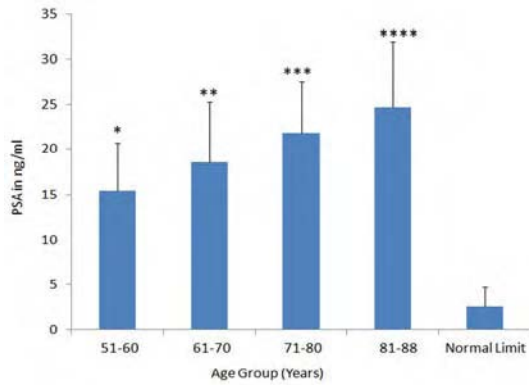


Figure 1. The elevated mean PSA level in different age group of patients

PSA was estimated in the blood samples of patients of different age group by CLIA. Each bar represents Mean \pm SD of the elevated PSA level of different patients in respective age groups. Statistical significance was compared with Normal limit by student t test. **** $p = 0.001$; *** $p = 0.005$, ** $p = 0.02$, * $p = 0.01$. [The data of 37 patients in (51-60), 51 patients in (61-70), 42 patients in (71-80) and 48 patients in (81-88) age group is shown as Mean \pm SD].

51 patients of 61-70 year age group were having very high level of PSA, the highest and lowest PSA level of this group were 28.7ng/ml and 11.1ng/ml respectively. 42 patients of the age group of 71-80 years were also having very high level of PSA, the highest and lowest PSA level of this group were 31.2ng/ml and 16.4 ng/ml respectively. Similarly, 48 patients had elevated level of PSA in the age group of 81-88 years, in which the highest and lowest PSA level of this group were 34.5 ng/ml and 15.2ng/ml respectively as shown in Fig.2.

The elevated mean value of PSA level of the patients in the age group of 51-60 years showed 15.4 ± 5.3 ng/ml, whereas the elevated mean PSA level of the patients in the 61-70 year age group showed 18.5 ± 6.8 ng/ml. The age group of 71-80 & 81-88 years had 21.8 ± 5.0 ng/ml and 24.7 ± 7.2 ng/ml as the elevated mean PSA level respectively.

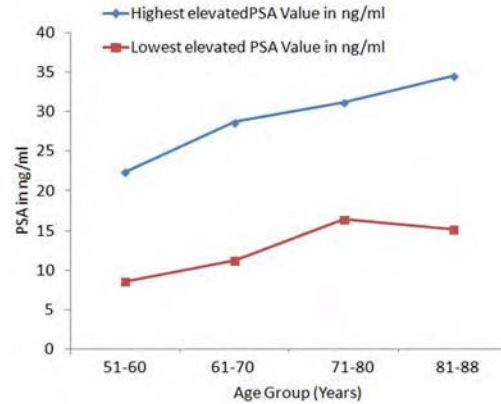


Figure 2. The highest and lowest PSA level in different group of patients

Blood samples of patients of different age group were tested for PSA level. The highest and lowest PSA level in all age group of patients, who showed elevated level of PSA.

The age group of 81-88 had more elevated mean PSA than the other age group as shown in Fig.1. The mean PSA of the total patients of all age group, who were having normal PSA level, was 2.6 ± 2.05 ng/ml as shown in Fig.1. The elevated PSA value (the data of 20 samples for each group) in patients of all age group is shown in scatter diagram in Fig.3.

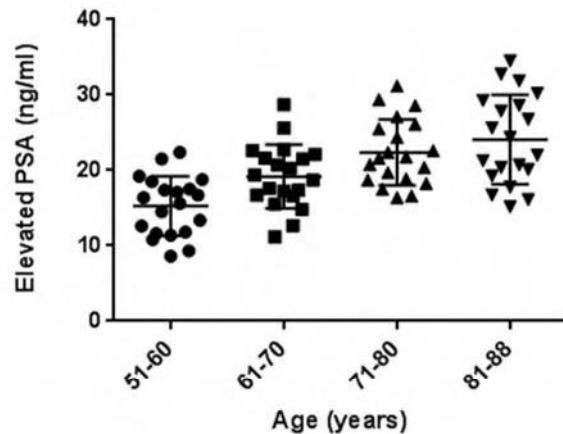


Figure 3. The elevated PSA value in different age group of patients

The blood samples of patients of the respective age groups were assayed for PSA level. The elevated PSA value in the different patients of all age group. (The data of 20 samples of each group is shown).

The normal level of PSA (the data of 20 samples for each group) in all age group of patients is shown in scatter diagram in Fig.4. Age group (51-60), (61-70), (71-80) & (81-88) had normal mean PSA value as 2.04, 2.46, 2.84 and 3.04 ng/ml respectively, as shown in Fig.4.

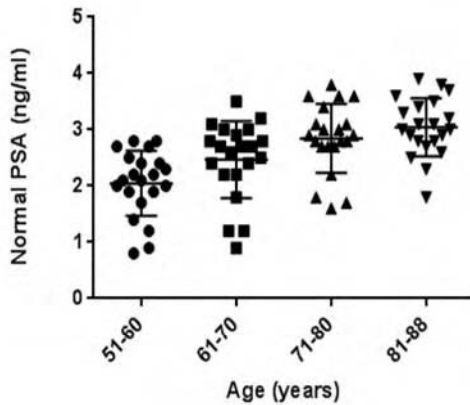


Figure 4. Normal level of PSA in patients of different age group

PSA level was estimated by the blood samples of patients of all age group. Normal level of PSA in the different patients of all respective age group. (The data of 20 samples of each group is shown).

Discussion

PSA is considered as the most valuable serum tumor marker for the successful diagnosis and post-surgical management of Pca. The improved rate of detection of prostate cancers has become largely possible because of routine use of PSA immunoassays. These days, PSA is measured in its various molecular forms and been employed in clinical practice [7,8].

Epithelial cells of all types of prostatic tissue, benign and malignant produce PSA. The peri urethral glands produce extra prostatic PSA, which is measurable in urine but cannot be detected in serum in women and in men. The liquification of the ejaculate, done by PSA, increases the motility of sperms [9]. The escape of high concentrations of PSA are generally restricted to general circulation by

Glandular ducts. In various disease conditions of the prostate, like prostate cancer, causes the increase of PSA outflow into the serum.

The present piece of work has been taken up with an objective to measure and compare the elevated diagnostic level of PSA in various patients with the normal PSA range obtained within the same patient population. The patients, screened for PSA, have been categorized into different age group and in all group it was seen that certain number of cases had significantly high level of PSA. The highest PSA value was upto 34.5 ng/ml, observed in age group of 81-88 years, as shown in Fig. 2. The highest mean PSA level was 24.5 ± 7.2 , observed in age group (81-88) as shown in Fig. 1. The mean PSA value of 49.8 ± 6.0 ng/ml has been reported in one study, which was carried out in Chinese men suffering with prostate cancer [10]. Our study revealed that 1692 patients of all age group were having PSA range within normal limit and the mean PSA of their normal range was 2.6 ± 2.05 ng/ml. In our present study, the normal mean PSA value of age group (51-60), (61-70), (71-80) and (81-88) were 2.04, 2.46, 2.86 and 3.04 ng/ml respectively as shown in Fig. 4.

While comparing our result with the reported cases from other countries, it seems to be similar with not much of significant difference. For example, the mean PSA value of patients of age groups (30-39), (40-49), (50-59), (60-69) and >70 has been reported as 0.86 ± 0.81 , 1.21 ± 0.6 , 1.59 ± 0.67 , 2.12 ± 0.84 and 2.76 ± 0.91 ng/ml respectively in prostate disease-free Chinese men population [10]. Similarly, the mean PSA value in Spanish workers without prostate problems in the age group of under 40 years, (40-49), (50-59) and (60-64) has been reported as 0.67 ± 0.49 , 0.77 ± 0.66 , 1.11 ± 1.22 and 1.57 ± 1.72 ng/ml respectively [11]. Age-

specific PSA reference level of men without prostate cancer in Japan and Iraq [12,13] has been also reported to be similar to that in China and Spain. Hence the reports of age-specific PSA reference level from various countries looks to be similar with the results of our present piece of study carried out in eastern part of Nepal.

The age-specific PSA reference range reflects the association between PSA and age. As men's age increases, the value of their serum PSA also increases. This is because of the enlarged prostate and increased leakage of the prostatic epithelium. It seems to be due to the subclinical inflammation or microscopic foci of cellular atypia [14].

In this present study, we can see in Figure 1 that the higher age group had more level of elevated mean PSA than lower age group. Elevated PSA value shown in scatter diagram in Fig. 3 also shows that higher age group had higher PSA value. Normal PSA value is also higher in higher age group. Normal mean PSA value of 81-88 age group is 3.04, which is more than normal mean PSA value of other age group as shown in Fig. 4. So the present study reveals that there is association between PSA level in serum and age of the patients.

Conclusion

PSA is used as a tool in the diagnosis and management of prostate cancer. However, the number of deaths related to prostate cancer diagnosed by PSA screening has appreciably decreased, it is dubious to say that this is only due to PSA. The distinction between the patients with prostate cancer from those without can't be done exactly by the level of PSA. Therefore, PSA screening programme has obviously assisted the diagnosis of many clinically insignificant prostate cancers and subsequent aggressive treatment with not much of clinical benefit. So in this study, we have shown the elevated and normal

range of PSA, in different age group of patients in eastern part of Nepal, which has got the significant value in the differential diagnosis of prostate.

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Original Article

Feto-Maternal outcomes in Intrahepatic Cholestasis in Pregnancy in a Tertiary Care Centre in Eastern Nepal

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Abstract

Background

Intrahepatic cholestasis of pregnancy has poor feto-maternal outcomes. To date there has been sparse publications regarding impact of intrahepatic cholestasis in feto-maternal outcomes in our setting. Therefore, we aimed to study the feto-maternal outcome in patients with intrahepatic cholestasis of pregnancy.

Material and Methods

A hospital based prospective cross-sectional study carried out in department of Obstetrics and Gynecology of Nobel Medical College, Biratnagar, Nepal from 1st January 2014 to 30th December 2015 in women who presented with pruritus in third trimester of pregnancy and having deranged liver function tests. All the cases were followed from admission to discharge. Socio-demographic, clinico-laboratory profile and feto-maternal outcomes were recorded in a preformed structured proforma. Descriptive statistics was used to present the data.

Results

Among 6,780 women admitted for delivery, 80 had cholestasis of pregnancy with incidence of 1.15%. 83% were of 18-35 years and 65% were primigravida. Most distressing symptom was generalized pruritus (75.0 %). The cesarean delivery rate was 46.25% and labor induction rate was (47.5%). Fetal complications were seen in majority of cases that included meconium aspiration syndrome 26 (32.5%), intrapartum fetal distress 21 (26.25%) and requirement of: intensive care 38 (48.75%). There were 7 perinatal and 3 neonatal deaths.

Conclusion

Intrahepatic cholestasis of pregnancy seems fairly common among pregnant women. It may be responsible for a large number of perinatal and neonatal deaths especially after 36 weeks of gestation. A large prospective study is needed to address the problems in time.

Key Words: *Feto-maternal outcome, Intrahepatic cholestasis in pregnancy, pruritus*

Introduction

Intrahepatic Cholestasis in pregnancy (ICP) is defined as pruritus with onset in pregnancy which is associated with abnormal liver function test in the absence of other diseases which resolves following

delivery. It typically occurs during third trimester of pregnancy and seldom occurs before 25 weeks period of gestation [1]. Its incidence varies in different countries and is very low in Europe (0.1 to 1.5%) whereas in Chile it is very high (14%) [2].

It is 1.2-1.5% in India and Pakistan [3]. Maternal consequences in ICP occurs due to increase in plasma protein concentration leading to alteration in carbohydrate metabolism and renal and intestinal function [4]. Steatorrhoea leading to deficiency in vitamin K dependent clotting factors and subsequent Post partum haemorrhage (PPH) has been reported [5]. In women of ICP, there is chance of 1.5 fold increase in cesarean delivery and 8 fold increase in duration of hospital stay for more than 10 days, 3 fold increase in induction of labor [6]. Adverse perinatal outcome is a major concern in intrahepatic cholestasis in pregnancy(ICP). The potential risks are fetal distress, intrauterine fetal death (IUFD), iatrogenic preterm delivery, meconium stained liquor, low birth weight and still birth [7 ,8]. Most distressing pruritus leads to sleep deprivation in pregnant women [9]. To the best of my knowledge, till this date, there are hardly any studies regarding this obstetric problem in our country. When data are extrapolated from different south Asian studies to our country, it is high likely that, ICP is common in our setting with poor fetomaternal outcomes. With this hypothesis, we aimed to study the fetomaternal outcomes in ICP in our setting.

Material and Methods

It was a Cross-sectional study design carried out in department of Obstetrics and Gynecology of Nobel Medical College, Biratnagar, Nepal from 1st January 2014 to 30th December 2015. Ethical clearance from institutional ethical review board (IERB) was obtained before conducting the study. Informed verbal and written consent was taken from the women before enrollment in the study. Any women with pruritus in 3rd trimester pregnancy underwent liver function test. Patients with history of itching and deranged liver function tests for which there was no

explanation other than pregnancy were included in our study. Every case was evaluated in detail, demographic, clinical and laboratory parameters were recorded in well-structured proforma. Cases were followed from admission to discharge.

All the maternal and fetal outcomes were noted. Information related to admitted newborn was obtained from neonatal intensive care unit(NICU). The collected data were entered in Microsoft Excel 2007 worksheet and statistically analyzed using the SPSS software version 11.5. Descriptive statistical data were presented as Mean, Standard Deviation, and percentage and proportions, and interquartile range, and the information were illustrated in graphical and tabular formats.

Results

During the one-year period, 6,780 women came for delivery and 87 had pruritus in third trimester. Liver Function test were abnormal in nearly 98% of the cases. Among them seven women were lost to follow up. The incidence of ICP was found to be 1.15%

Table 1: Demographic characteristic of patients

Characters		Number (n = 80)	Percent
	< 18 years	8	10
	18-35 yrs	67	83.7
Age	> 35 yrs	5	6.25
Gravidity	Primigravida	52	65
	Multigravida	24	30
	Grand multigravida	4	5
		Total 80	

Sixty-seven (83.7%) of the cases were in the age group of 18-35 years. Fifty-two (65%) were primigravidas and 24 (30%) were multigravida. All women were presented with complain of whole body itching more in palm and sole however 60(75%) women were having severe itching leading to disturbed sleep. While

analyzing past obstetric history, out of 80 women 11(13.7%) had history of previous pregnancy loss. Out of them ,4 (5%) had history of early pregnancy loss whereas remaining 4(5%) had history of intrauterine fetal death and 3 gave history of fresh still birth. Among 7 women of late pregnancy loss, only 3 (3.75%) women gave history of itching in palm and sole but none of them sought medical advice for this complain.

All 4(5%) cases of IUFD had reached hospital with history of not perceiving fetal movement for more than 24 hours. The 3 (3.75%) cases of fresh stillbirth had reached hospital in previous pregnancy with history of per vaginal leaking but not associated with pain at 38- 39 weeks period of gestation. While analysing gestational age at onset of pruritus, 38 (47.5%) women had onset at 32 -36 weeks period of gestation whereas 22 (27.5%) had onset at 28-32 weeks period of gestation. 11(13.75%) women had onset of pruritus at 24-28 weeks period of gestation and 9 (11.25%)women had after 36 weeks period of gestation. None of the women gave history of pruritus before 24 weeks period of gestation.

Table 2 : Liver Function Tests

Parameters	Value	Percentage of women
Alanine aminotransferase(ALT)	38-650 IU/L	97.8
Aspartate aminotransferase(AST)	40-640 IU/L	97.8
Alkaline phosphatase	70-1890 IU/L	45.5
Total Billirubin	1.0 - 3.8 mg%	11

Among 5 cases of Intrauterine fetal deaths, 3 were admitted with complain of whole body itching since 10 to 15 days and not being able to perceive fetal movement at 37-38 weeks' period of gestation. While

remaining 2 admitted with labor pain and on further asking gave history of itching particularly in palm and sole. All 5 cases were unbooked.

Table 3 : Gestational age at delivery

Weeks of Gestation	Number (n= 80)	Percent
<34 weeks	9	11.2
34-36 weeks	24	30
37-40 weeks	41	51.25
>40 weeks	6	7.5

Table 4 : Complications of pregnancy

Complications	Number n= 80	Percent
PPROM	5	6.25
Preterm delivery	15	18.7
PROM	8	10
Elective caesarean section	8	10
Emergency caesarean section	29	36.25
Postpartum Haemorrhage	9	11.25

Table 5 : Neonatal outcome

Outcome	Number n= 80	Percent
APGAR score <7 at 5 minutes	11	13.75
Birth weight in grams <2500 grams	18	22.5
Intrapartum fetal distress	21	26.25
Meconium stained liquor	26	32.5
Spontaneous preterm delivery	8	10
Intrauterine fetal death	5	6.25
Fresh still birth	2	2.5

Out of 80 neonates, 38(48.75%) neonates were admitted in NICU. The causes of neonatal admission was preterm for supportive care 6(7.5%), presumed sepsis in 7(8.75%), neonatal sepsis 5(6.25%), meconium aspiration syndrome in 13(16.25%) and birth asphyxia 8,(10%) . There were 2 (2.5%) cases of fresh stillbirth; both the cases had undergone induction for obstetric cholestasis with

postdated pregnancy. Out of 38 cases of NICU admission, 1 case went home against medical advice on second day of delivery, 3 cases had neonatal death and remaining 34 cases were discharged after treatment. Among 3 cases of Neonatal death, 2 were admitted for meconium aspiration syndrome and remaining one for presumed sepsis.

Discussion

This prospective study describes the fetomaternal outcome of obstetric cholestasis in referral center of Eastern Nepal. During the study period, there were 6,908 women admitted for deliveries. The incidence of obstetric cholestasis was 1.15% which is comparable to the previous study done by Sultana and her colleagues [3]. In our study 38(47.5%) of women were induced which is almost similar to study done by Turunen et al [6]. Eight (10%) women were induced at 34-36 weeks period of gestation for increasing level of liver enzymes despite medical treatment with ursodeoxycholic acid. However, 17(21.25%) women were induced at 37-38 weeks period of gestation for persistent pruritus though liver parameters were improving. Six women (7.5%) went induction postdated as they were lost in follow up and were admitted after crossing 40 weeks period of gestation only and rest 7(8.75%) women were induced at 38-40 weeks period of gestation. Out of 25 cases (31.25%) of early induction i.e. before 37 weeks, 11 women (13.75%) underwent cesarean delivery for failed induction. In our study, out of 80 women, 46.25% underwent cesarean section, out of which 10% were elective cesarean section and 36.25% emergency cesarean section. It is comparatively higher than previous study [6] (14.8%), the reason maybe we had gone for early induction in 31.25%, so increased rate of cesarean for failed induction 11(44%). In our study 11.25%

women had postpartum hemorrhage whereas Wang et al (2010) found it to be 1.4% [10]. The reason for high incidence of PPH in our study is attributed to high incidence of anemia in our area, poor antenatal visits and low socioeconomic status and only 72% of women had injecton vitamin k before delivery.

While analyzing Neonatal outcomes the incidence of low APGAR score <7 in 5 minutes was in 13.75% which is almost similar to previous study done by Alokanda et al in 2005 (18.5%) [2]. However, it is very high (4.4%) when compared with next study done in India [11]. The reason maybe we have 87% unbooked obstetric cholestasis cases and their higher rate of cesarean section (93.3%). The disease has been related to a high incidence of perinatal complications leading to 45 % meconium stained liquor, 44% preterm delivery and higher incidence of fetal distress (upto22%) [12,13].

It is suggested that both intrapartum fetal distress and increase incidence of meconium stained liquor is due to the stimulation of colonic motility by bile acids on Obstetric Cholestasis [13]. Like other study [14] (33.3%) we have also observed higher incidence of meconium stained liquor in 32.5%. But Padmaja M et al had not shown significant incidence of meconium stained liquor, which is attributed to proper antenatal visit leading to on time intervention of Obstetric Cholestasis [11].

In our study we observed that 15(18.75%) were preterm (iatrogenic 7 and spontaneous 8) which is almost similar to study done by Roncaglia N et al showing incidence of 19.5% [15]. Our study had similar finding 6.25% to previous study by Sultana et al 6.67% in relation to intra uterine fetal death [3]. But it is high when compared to study done by Alokanda [2] where incidence of IUFD was found to be only 3.1% which is attributed to our poor number of booked cases and all 5 cases

had intrauterine fetal death before being admitted in hospital. We found only two (2.5%) case of fresh stillbirth like in study done by Turunen et al [6] (1.2%) where as another study done in India [11] had shown very low i.e only 0.02% which is attributed to booking status, good antepartum care and higher incidence of cesarean section. In a study conducted by Zecca E and colleagues, IUFD was found to be in 6% patients which is similar to our study (6.25%) [16].

We had 38(47.55%) NICU admissions which are comparatively higher than study done by Deveer et al where the incidence was only 27% [17] which is due to higher number of intrapartum fetal distress and higher percentage of meconium stained liquor (32.5%) in our study. Another study by Sebiha et al had also found almost similar to our finding where incidence of meconium stained liquor to be 25-45%, preterm labor 44% and IUFD upto 5% [18]. Obstetric cholestasis is associated with premature delivery both spontaneous and iatrogenic and increase incidence of IUFD and the perinatal mortality from Obstetric Cholestasis is 10.6\1000 live birth [19]. Intrauterine fetal death is usually sudden and seems to be due to Acute anoxia [20].

Conclusion

Intrahepatic cholestasis of pregnancy seems fairly common among pregnant women in our setting. It was found to be responsible for a large number of perinatal and neonatal deaths especially after 36 weeks of gestation. A large prospective study is needed to find the clinic-epidemiological pattern of this obstetric problem. In the mean time, it is important to realise that by increasing awareness among the health personnel caring for the pregnant women that pruritus of pregnancy is a high risk condition and close fetal monitoring and timely intervention will decrease perinatal mortality significantly.

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Original Article

Clinical Characteristics and Endoscopic Findings of the Patients with Cirrhosis of the Liver in a Tertiary Care Centre in Eastern Nepal

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Abstract

Background

Studies on clinical characteristics and upper gastrointestinal endoscopic findings of the cirrhotic patients in a tertiary care centre are sparse from eastern region of Nepal. The aim was to profile these patients clinically and analyse the endoscopic findings.

Material and Methods

This was a cross-sectional analytical study carried out in the Department of Medicine of Nobel Medical College, Biratnagar from 30st September 2012 to 30th August 2013 (one year). After admission, detail medical history and meticulous clinical examination was carried out in every patient with clinical diagnosis of cirrhosis of liver. Routine, biochemical, hematological, imaging and special investigations were sent as per clinical scenario. Upper gastrointestinal endoscopy was carried out in all patients. Basic descriptive statistics were used to present the data.

Results

A total of 104 patients were enrolled in our study. The mean age was 50.09 years \pm 11.79 (Range 26-79), of which 60% were males. Almost 70% of the patients were from productive age group (31-70 years). All the patients were symptomatic. Chronic excessive alcohol consumption was the commonest cause of cirrhosis (80.76%). The major clinical presentations were ascites (83.65%) and jaundice (79.92%). Pedal edema was the commonest (85.6%) presenting sign. Diabetes mellitus and pneumonia were common comorbidities. Gastroesophageal varices were commonest (70.19%) endoscopic finding.

Conclusion

Cirrhotic patients presented late with complete decompensation in the form of ascites, jaundice and upper gastrointestinal bleeding from esophageal varices. Mostly people with productive age group were affected.

Key Words: *Clinical characteristics, cirrhosis, endoscopic findings*

Introduction

Cirrhosis of liver is a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules [1]. This has emerged as a major cause of global health

burden. It was the cause of 31 million Disability Adjusted Life Years (DALYs) or 1.2% of global DALYs, in 2010 [2]. Cirrhosis is among the top causes of death and kills nearly 150,000 people worldwide each year. Alcoholic cirrhosis accounts for

nearly (38-50%) of all cirrhosis related deaths. It is the third leading cause of death in people aged between 25-65 years exceeded only by cardiovascular diseases and cancer [3]. In Nepal, chronic alcohol abuse is a major public health problem and is the commonest cause of the cirrhosis of the liver [4]. Portal hypertension is the major complication and is responsible for the upper gastrointestinal (UGI) bleeding, ascites, hepatorenal syndrome and hepatic encephalopathy. Clinically significant portal hypertension is defined above threshold of 12 mm Hg. Bleeding from the esophageal varices is the most serious complication of portal hypertension with high morbidity and mortality [5,6]. Prospective studies have shown that more than 90% of the patients with cirrhosis will develop oesophageal varices sometime in their life and 30% of them will bleed [7,8]. Variceal haemorrhage accounts for (10-30%) of all cases of UGI bleeding and accounts for 80-90 % of bleeding episodes in cirrhotic patients [9,10]. Apart from variceal bleeding, cirrhotic patients bleed 7% episodes from gastric varices, and (5-20%) form congestive gastropathy. peptic ulcer, Mallory-Weiss tear and other sources account for the remainder [11].

Gastroesophageal varices are the commonest cause of upper gastrointestinal bleeding in cirrhotic patients [12]. UGI endoscopy is the primary modality for determining the cause of bleeding in case of cirrhosis.

To the best of my knowledge, the studies regarding the clinical profile and endoscopic findings of the patients with cirrhosis of liver are sparse in eastern region of Nepal. The aim of the study was to analyze clinical and endoscopic profile of these patients in our setting.

Material and Methods

This was a cross-sectional analytical study carried out in Department of Medicine of Nobel Medical College, Biratnagar from

1stOctober 2012 to 30thSeptember 2013 (one year). After admission, detail medical history and meticulous clinical examination were carried out in every patient with clinical diagnosis of cirrhosis of liver. Routine biochemical, haematological, imaging and special investigations were sent as per clinical scenario. Upper gastrointestinal endoscopy was carried out in all patients. The collected data was entered in Microsoft Excel 2013 and converted into Statistical Software Package for Social Sciences (SPSS 11.5 version) for statistical analysis for descriptive statistics. Percentage, Mean, Median, Standard deviation (SD) and Interquartile range (IQR) were calculated and tabular and graphical presentation made accordingly.

Results

During the period of one year, a total of 104 patients with cirrhosis of liver were enrolled in our study.

Socio-demographic characteristics

The mean age was 50.09 years ± 11.79 (Range 26-79), of which 60% were males. Almost 70% of the patients are from productive age group (31-70 years). Most of them (60%) were agricultural workers and more than 80% patients did not have formal education.

Table 1: Age distribution of the study subjects

Age (years)	Number	Percentage
Less than 30	6	5.77
31-40	21	20.19
41-50	28	26.92
51-60	24	23.08
61-70	20	19.23
More than 70	5	4.81

Table 2: Symptomatology of the study subjects

Presentations	Number	Percentage
Ascites	87	83.65
Jaundice	80	79.92
UGI Bleeding	48	46.15
Hepatic encephalopathy	31	29.8
Fever	31	29.8

Spontaneous bacterial peritonitis(SBP)	27	25.96
Hepatorenal syndrome	10	9.6

Nearly 80% of the patients have ascites and jaundice during presentation.

Table 3: Clinical signs

Clinical signs	Number	Percentage
Pedal edema	89	85.6
Splenomegaly	61	58.6
Pallor	50	44.2
Hepatomegaly	40	38.4
Asterixis	36	35.0
Spider angioma	36	35.0
Pubic/axillary hair loss	34	32.7
Palmar erythema	18	16.9
Clubbing	13	12.5
Gynecomastia	12	11.5
Parotidomegaly	11	10.5
Testicular atrophy	11	10.5
Breast atrophy	5	4.8
Caput medusa	3	2.9

Most of them (85.6%) have pedal edema.

Table 4: Etiology of cirrhosis

Etiology	Number	Percentage
Chronic alcohol consumption	84	80.76
Hepatitis B virus infection(HBV)	6	5.76
Hepatitis C virus infection(HCV)	3	2.88
Alcohol and HCV	2	1.92
Alcohol and HBV	1	0.96
Unknown	8	7.69

Almost (81%) have ethanol induced cirrhosis

Table 5: Co-morbidities

Co-morbidity	Number	Percentage
Diabetes mellitus	7	6.7
Pneumonia	6	5.8
COPD	4	3.8
Pulmonary tuberculosis	3	2.9
Hypertension	2	1.9
CVA	2	1.9
HIV	1	0.96
IHD	1	0.96

Diabetes mellitus and pneumonia are common comorbidities in cirrhotic patients.

Table 6. Endoscopic findings

Endoscopic findings	Number	Percentage
Gastroesophageal varices	73	70.19
Gastric ulcer	6	5.76
Duodenal ulcer	6	5.76
Portal hypertensive gastropathy	4	3.84
Fundal varices	2	1.92
Erosive gastritis	2	1.92
Normal endoscopy	11	10.57

Most of the patients (70.19%) have gastroesophageal varices followed by normal UGI endoscopy in (10.57%) patients. When patients were classified according to modified Turcott Child Pugh classification, it was found that Class A (25%), class B (45%) and class C (30%).

Discussion

During one-year period, 104 patients were enrolled in the study. Mean age of our patient was 50.09 ± 11.79 years (26-79) which corroborates with previous two different studies [13,14] who found mean age of 51.7 ± 11.3 years. Other two studies [15,16] found mean age of 57 ± 9 years (30-76) and more or less similar finding were also reported by Dinis-Riberio M et al [17] and Mihas AA et al [18]. This shows that people with productive age group are affected most. In our study, 60% patients were males. This male predominance as such may be due to social and cultural background of our society where alcohol consumption by males is accepted to some extent. In the study done by Fillik L et al [19], (69.6%) were males and Coral GP et al, [20] reported (76.59%) males in their study. Arsad KB et al [13] found (65%) males and Okeke EN et al [21] found (80%) males in their studies. Singh V et al [22] in India found (70%) to be males and Muhammad AN et al [23] found that (68%) were male in their study. This was a surprising finding in our study that the number of males is less as compared to above studies because in

eastern region consumption of alcohol by female is socio-culturally accepted in certain ethnic groups which might have contributed to bulk of our cirrhotic patients. Regarding symptoms during presentation, we found ascites in (83.65%) cases, UGI bleeding (46.15%), jaundice (79.92%), hepatic encephalopathy (29.8%), spontaneous bacterial peritonitis (SBP) in (25.96%), fever (29.8%) and hepato-renal syndrome (9.6%). In a study done by Arsad KB et al [13], involving 282 patients, it was found that (57%) presented with UGI bleeding, (47%) with hepatic encephalopathy, (9%) with hepatorenal syndrome. Muhammad AN et al [23] studied 100 patients and following symptoms were noted during presentation, ascites (76%), jaundice (41%), hepatic encephalopathy (38%), UGI bleeding (42%) and fever in (24%). Another study done by Bell H et al [24] in Norway including 100 patients found ascites in (67%) and UGI bleeding (34%). Tung T et al [25] found haematemesis as presenting symptom in (15-25%) and fever (35%). Bunay KD et al [26], studied 45 patients and ascites was noted in (73.3%), UGI bleeding (40%) and hepatic encephalopathy (24.4%). Mihas AA et al [18] reported fever in (54%), hepatic encephalopathy (67%). In other study Pelletier G et al [27] found UGI bleeding in (42%), hepatic encephalopathy (50%). In the study by Fillik L et al [19], jaundice was present in (54.5%), hepatic encephalopathy in (50.7%), and fever in (38.8%). In the study by Iqwal S et al [28] (65.6%) had jaundice, (54.9%) had encephalopathy and 19.6 had UGI bleeding. Nadeem MI et al [16] found jaundice in (64%) and hepatic encephalopathy in (19%). The above variation in patient's clinical characteristics reported by different studies is probably due to variation in study methodology, geographical location and social-cultural

background of the study population. Regarding stigmata of chronic liver disease, pedal edema (89%) was the commonest presentation followed by splenomegaly (61%) and pallor (50%) in our study. Nadeem MI et al [16] reported pedal edema in (92%), clubbing (25%), palmar erythema (25%), testicular atrophy (4%), gynecomastia (4%), pubic hair loss (2.4%), parotidomegaly (1.2%), spider naevi (1.2%). Tung T et al [25] found hepatomegaly in (70%), splenomegaly 35-50%. In our study, chronic alcohol abuse was the commonest cause of cirrhosis (80.76%) followed by chronic hepatitis B virus infection (5.76%) and chronic hepatitis C virus infection (2.8%). In nearly (8%), no cause was found. During the investigation of etiology of the cirrhosis, not all the patient afforded all investigations and few tests were unavailable. Rare cause might have been missed and included in the cryptogenic group. Walsh K [29] found alcohol as a cause of cirrhosis in 80% cases. Morea Ret al [30] found alcohol as cause in (67%), chronic hepatitis C in (15%), combination of chronic hepatitis C and alcohol in (15%) and chronic hepatitis B in (3%). Riepe SP et al [31] reported alcohol as cause in (65%). Mendez-sanchez N et al [32] found alcohol in (39.5%), chronic hepatitis C in (36.6%), chronic hepatitis B in (5%) and cryptogenic in (10.4%). Some of the above findings corroborate with ours whereas some findings do not. Chronic viral infections are increasing in our society adding on or replacing alcohol as a major cause of cirrhosis. Diabetes mellitus, pneumonia and ischemic heart disease were common comorbidities in our study whereas Morea R et al [30] found hypertension, diabetes and ischemic heart disease as common comorbidities in their study. In our study of UGI endoscopic findings, gastro-oesophageal varices were noted in (70.19%) of the patients,

congestive gastropathy (3.84%), gastric ulcer (5.8%) and normal (10.57%). Bunay K D et al [26] found gastro-oesophageal varices in (93.3%). Khuram M et al [33] studied 299 patients who underwent UGI endoscopies and gastro esophageal varices were found in (84.6%) patients. They also noted congestive gastropathy in (11%), gastric ulcer in (0.2%), normal endoscopic findings in (14.7%) which is probably due to larger number of cases in their study. Eighteen percent patients died in hospital in our study, the death rate could have been higher because few serious patients left hospital without medical advice and few referred to other centers because of various reasons.

Conclusion

Most of the patients presented late in decompensated state and many were continuing to consume alcohol just before hospital visit which is preventable cause of cirrhosis. Properly planned health education regarding harmful effects of alcohol and hepatitis B and C infection should be implemented in the community.

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Original Article

Evaluation of Prescription Pattern and Rational Prescribing in Eastern Nepal

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ABSTRACT

Background

To promote rational prescribing and appropriate use of drugs, it is important to evaluate the prescription pattern using the World Health Organization (WHO) drug use indicators. The aim of this study was to evaluate the prescription patterns and rational prescribing at the private community pharmacies of Biratnagar, Eastern Nepal, using some of the WHO core drug use indicators.

Material and Methods

Five private community pharmacies were selected using systemic random sampling. Nine hundred patient encounters from these pharmacies were assessed prospectively for four months from September 2015–December 2015. Data was collected from each patient encounter and were recorded directly into a prescription indicator form.

Results

Average number of drugs prescribed per encounter was 2.14 (n=1930). Percentage of drugs prescribed by generic name and from essential drug list was 45.18% (n=872) and 76.11% (n=1469) respectively. Percentage of encounters in which antibiotic and injection was prescribed were 40.44% (n=364) and 3.44% (n=31) respectively.

Conclusion

Prescribing practices in Eastern Nepal are not up to the standards recommended by WHO. Drug use evaluation can help to ensure whether the antibiotics are appropriately prescribed or not. Poly-pharmacy, excessive use of antibiotics was quite common and concept of generic prescribing and National Essential Medicine List (NEML) was not appreciable. Standard guidelines should be recommended and strictly followed by the prescribers and National Formulary and NEML should be made available in every health institution. Physicians should be emphasized to prescribe medicines from NEML.

Key Words: *Drug use indicators, Prescription pattern, Rational prescribing*

Introduction

Quality of health and medical care amongst the patients and the community is determined by the rational prescribing and appropriate use of drugs [1]. Study in Nepal has revealed excessive use of

antibiotics, prescribing of large number of drugs and injections are common drug use problems [2]. World Health Organization/ International Network for Rational Use of Drugs (WHO/ INRUD) have forwarded indicators as measures of performance in

general areas related to rational use of drugs. WHO states that 100% of the medicines must be prescribed from the Essential Medicine List of any country [3]. Studies conducted in Nepal show that essential medicines are widely prescribed more in health facilities than in private practice. DDA's study on 'Drug Prescribing habits in Private Practice in Kathmandu Municipality area' shows drugs prescribed from EML is 32.4% and at Zonal hospital is 42% [4]. For the effective promotion of rational drug use in developing country it is essential to assess the compliance of drug use pattern with WHO drugs indicators [5]. So, knowing where and when errors in rational prescribing are most likely to occur is the first step in trying to prevent these errors.

This study was conducted to assess drug use pattern in Eastern Nepal using WHO Prescribing Indicators so as to promote rational use of drugs. Considering the vital role of appropriate formal prescriptions in medical practice, and for better health care delivery system, this study is conducted to create awareness of rational use of drugs, prescribing drugs from essential medicine list. This can be achieved by assessing the prescription patterns of different private community pharmacies with the standard WHO prescribing indicators. Thus the result of this study proves to be useful for the prescribers to understand the importance and need of emphasizing on the adherence to the standard WHO prescription format.

Material and Methods

Five private community pharmacies of Biratnagar were selected using systemic random sampling method. Ethical approval from the Institutional Review Community was taken. Prescriptions of ambulatory adult patients of all categories of diseases and age group were analyzed from September 2015 to December 2015. Prescription of patients visiting for follow up or prescriptions of patients at the time

of discharge were not taken into consideration. With reference to WHO Core Prescribing Indicators, data needed to measure the prescribing pattern was collected and recorded for each patient encounter and entered directly into a prescribing indicator form. Essential Medicines WHO Model list (2015) and National List of Essential Drugs, Nepal (2011) were used to find the percentage of drugs from essential drug lists.

The WHO Prescribing indicators were measured included:

1. Average number of drugs per encounter.
2. Percentage of drugs prescribed by generic name
3. Percentage of encounters with antibiotic(s) prescribed.
4. Percentage of encounters with injection(s) prescribed.
5. Percentage of drugs prescribed from an essential medicine list (EML).

Results

Nine hundred prescriptions were evaluated from the private community pharmacies of Biratnagar, Nepal. Most prescriptions were for females (68.55%), with a mean age of 33.3 years. Total of 1930 drugs were prescribed. Average number of drugs prescribed per prescription was 2.14. Total number of drugs prescribed by generic name was 872 (45.18%). An antibiotic was prescribed in 364 patient encounters (40.44%) Most of the drugs prescribed (n = 1469, 76.11%) were on the essential list of Nepal (Table1).

Table 1: Results obtained at private community pharmacies of Biratnagar.

Prescribing indicators	Total drugs / encounters	Average / percent
Average number of drugs per encounter	1930	2.14
Percentage of drugs prescribed by generic name	872	45.18
Percentage of	364	40.44

encounters with an antibiotic prescribed		
Percentage of encounters with an injection prescribed	31	3.44
Percentage of drugs prescribed from essential drug list	1469	76.11

Of total 1930 drugs prescribed, 831 (43.05%) were antibiotics. The most commonly prescribed antibiotics were cefixime (19.61%), amoxicillin (19.13%), azithromycin (14.07%), ciprofloxacin (11.55%), cloxacillin (10.46%). (Table 2)

Table 2: Commonly prescribed antibiotics at the private community pharmacies of Biratnagar.

Commonly prescribed antibiotics	Frequency	Percentage (%)
Cefixime	163	19.61
Amoxicillin	159	19.13
Azithromycin	117	14.07
Ciprofloxacin	96	11.55
Cloxacillin	87	10.46
Ampicillin	45	5.41
Metronidazole	44	5.29
Ofloxacin	37	4.45
Gentamycin	21	2.52
Cefadroxil	20	2.40
Cefalexin	16	1.92
Nitrofurantoin	12	1.44
Ceftriaxone	9	1.08
Levofloxacin	5	0.60
Total	831	99.93

The percentage of encounters in which an injection was prescribed was 3.44%. The most commonly prescribed injections were ceftriaxone (29.03%), diclofenac sodium (25.8%), tetanus toxoid (19.35%), multivitamin (9.67%) (Table 3).

Table 3: Commonly prescribed injections at the private community pharmacies of Biratnagar.

Commonly prescribed injection	Frequency	Percentage (%)
Ceftriaxone	9	29.03
Diclofenac	8	25.8
Tetanus toxoid	6	19.35
Multivitamin	3	9.67
Dexamethasone	3	9.67
Metronidazole	2	6.45
Total	31	99.97

Discussion

Irrational use of drug occurs in all countries and cause harm to people [6]. In this study, WHO/INRUD drug use indicators were basically used to assess the current prescribing pattern so as to facilitate the rational use of medicine in populations.

This study shows the average number of drugs per encounter was 2.14 (Table 1). The average number of drugs per encounter recommended by WHO is 1.6 to 1.8 [7]. In similar study conducted in PHC facilities of Kathmandu the average number of drugs per prescription was 1.5 [8]. The average in this study deviates the standard provided by World Health Organization and exceeds that of PHC facilities as well. This can be due to the tendency of prescribing more drugs by the prescribers in private practices due to various reasons. This can lead to poly-pharmacy, increased risk of drug interaction, non-compliance and irrational drug use.

WHO recommends 100% of drugs to be prescribed generically [7]. This study shows the percentage of medicines prescribed generically is 45.18 (Table 2) which goes hand in hand with the results of the study (44%) conducted in PHC facilities of Kathmandu [8]. In some of the developing countries, this value was > 59% [9, 10]. Study conducted in the Western Nepal revealed it to be 63.5% [11]. Thus, it is found that effective implementation of the existing policy of generic prescribing is not satisfactory in Eastern Nepal. This can lead to increased cost of drugs, chances of generic duplication leading to the adverse effect and drug related toxicity, and unethical marketing by some industries.

Thus, the policy on generic prescribing in Nepal has to be strictly followed by the prescribers. The prescribers should remain adherent to the national guidelines and the WHO guidelines on rational prescribing of drugs.

WHO recommends percentage of encounters with antibiotic prescribed should be 20.0% to 26.8% [7]. In this study, the percentage is 40.44% (Table 1) and accounts for 43.05% of total drugs prescribed. Although it is consistent with the 43% of encounters revealed from the study conducted in the PHC facilities of Kathmandu [8] the average is between 29% and 43% in developing countries. In Nepal, 52.4% of patients received at least one antibiotic in terai districts whereas the percentage was 45.2% in hilly districts [2]. PHC is usually provided by the government through national health care systems whereas private health care can be provided through for profit hospitals and self employed practitioners. This can be the reason of increased percentage of antibiotics prescribed in this study.

Although the WHO standards for encounters with injection are 13.4 – 24.41% [7], this study revealed it to be 3.44%. Previous study in Nepal revealed 8.8 percent of encounters in terai region and 3.2 percent in hilly region received injections [2,4], in PHC facilities of Kathmandu it was 5% [8]. Percentage of encounter with an injection prescribed is better if it is as low as possible because of the risk of communicating diseases and the increased use of health care resources. The current trend of prescribing limited number of injections should be continued and should not be higher than the standard limits.

WHO states 100 percent of drugs should be prescribed from Essential Medicine List of any country [7], but in this study only 76.11% of drugs are prescribed from EML, 2015. In previous study 75.6 percent of drugs were prescribed from the EML [9]. There is need to increase the number of medicine prescribed as per EML so as to match the WHO standards. The prescribers should remain updated about the WHO Model List of EML of the country so as to

follow the standards and to avoid the chances of irrational use of drugs, poly-pharmacy and thus achieve better health care delivery.

Our study had a number of limitations. The study could not cover all the health facilities and could not reveal the exact reason that led to poly pharmacy, excessive use of antibiotics and less adherence to the NEML.

Conclusions

The percentage of encounters with injection prescribed was lower than that reported elsewhere. This is to be encouraged. Other prescribing practice is not up to the standards recommended by WHO. Irrational practice of prescribing the drugs is common. Poor compliance of physicians with WHO Core Prescribing Indicators may lead to undesired drug effects, toxicities, tolerances and resistances. Excessive use of antibiotic is common and the trend of prescribing medicines from NEML is not up to the mark. Further studies for a longer period of time in a greater number of pharmacies, health facilities are required.

Regular workshops, seminars, training should be encouraged by the regulatory agencies to promote the value of core prescribing indicators of WHO. Standard guidelines should be recommended and strictly followed by the prescribers and National Formulary and NEML should be made available in every health institution. Physicians should be emphasized to prescribe medicines from NEML.

Thus, standard prescribing pattern and compliance with WHO Core Prescribing Indicators can be guaranteed and rational prescribing can be promoted.

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Original Article

Comparison of General versus Spinal Anesthesia in Patients undergoing Percutaneous Nephrolithotomy: A Prospective Randomized Study

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Abstract

Background

Percutaneous Nephrolithotomy, widely used procedure by urologists for removing renal stones nowadays. Generally, it is preferred in general anesthesia but here in our study we have compared it with spinal anesthesia to know its safety and efficacy.

Material and Methods

Sixty patients of either sex, aged between 20-60 years, ASA – Grade I and II, with stones size larger than 15 mm posted for Percutaneous Nephrolithotomy were randomly selected. Patient was divided in two groups 30 each, Spinal Anesthesia (S) and General Anesthesia (G). Patient's stones sizes, numbers & location, Anesthesia duration, Surgical duration, Recovery duration, Blood loss and Blood transfusion, Analgesic demand, post-operative Nausea & Vomiting, Patient satisfaction, Hospital stays and Heart Rate and Mean arterial pressure between two groups were compared.

Results

There was no significant difference in terms of mean age, weight, stones sizes, numbers and its location. The p value for Anesthesia duration and surgical duration were 0.144 and 0.22 which was insignificant. Recovery duration (p-value 0.007), Blood loss (p-value 0.004) were significantly lesser in spinal anesthesia group. There was no significant difference in nausea and vomiting, patient satisfaction when compared between two groups. But Analgesic demand, Blood Transfusion and Hospital stays significantly found to be decreased in spinal anesthesia groups ($p < 0.05$). The mean of MAP showed no significant difference except in 10 and 20 minutes.

Conclusion

Spinal anesthesia tends to be as effective as general anesthesia for PCNL and beneficial in terms of recovery duration, blood loss, analgesic demands, hospital stays, hence decrease the cost of patient.

Key Words: *General anesthesia, Percutaneous Nephrolithotomy, Renal stones, Spinal anesthesia*

Introduction

Percutaneous nephrolithomy (PCNL) is one of the most popular techniques to remove the renal stones in today's world. Its

popularity is increasing day by day due to its less hospital stay, less scar marks, less post operative pain, fast ambulatory. Surgical Stages for PCNL are classified as

Renal access, Tract dilatation, Nephroscopy & Stone disintegration and Nephrostomy tube insertion [1]. General anesthesia during PCNL enables control of ventilation and also subjected to comfort of patients [2]. Therefore, choice of anesthesia mostly chosen by anesthesiologists is general anesthesia [3]. But, Anesthetics complications and patient's costs seems to be higher with general anesthesia when compared with spinal anesthesia [4].

Hence, some of the previous studies shown that PCNL with spinal anesthesia have better outcomes in comparison with general anesthesia [5]. Neuraxial block like spinal, epidural has advantage over general anesthesia in many urogenital surgeries including PCNL and is a choice of anesthesia in patients who are at high risk for surgery under general anesthesia [6]. In this study, comparison between spinal & general anesthesia has been done in PCNL, its surgical outcomes and complications to know which one has better outcome.

Material and Methods

The study was conducted at Nobel Medical College Teaching Hospital Pvt. Ltd, Biratnagar, Nepal, during the period of 15th April 2015- 15th April 2016.

This Randomized, prospective clinical study was conducted on 60 adults, ASA- Grade I & II patients, aged between 20 to 60 years of either sex, stones larger than 15 mm posted for PCNL in Urology Operation Theatre. After approval, informed consent taken, patients were randomly divided into two groups of 30 each.

Group G- General Anesthesia group

Group S- Spinal Anesthesia group

Exclusion criteria for this study were any contraindication for spinal anesthesia, ASA – Grade III or above, any congenital anomalies of kidneys like Ectopic or horse shoe kidneys, coagulation disorders.

Pre-Anesthetic evaluation was done after taking proper history with systemic

examination and relevant investigations were advised. Beside Routine preoperative investigation complete blood count (CBC), Renal function test, Coagulations profiles and routine urine examination was done in all patients. X-ray KUB and Intravenous pyelography was done to locate the position of stone and its size.

Anesthetic Management

On arrival in the operation theatre IV line was secured and all the baseline monitors like NIBP, ECG & SPO2 were attached and recorded. In Group G patient's premedication were done with glycopyrolate 0.1 mg & midazolam 0.04mg/kg. After premedication Inj fentanyl 1mcg/kg was given in this group patient. Pre-oxygenation was done for 3 minutes and induction was done with Inj propofol 2.5mg/kg & Inj. Atracurium 0.5mg/kg. Then the patient was intubated with appropriate endotracheal tube and fixed the tube. Maintenance was done with Isoflurane & Atracurium with oxygen. Patient was made prone after stabilization of anesthesia and cystoscopy and urethral catheterization was done on lithotomy position. HR, SPO2, SBP, DBP, MAP were recorded through-out the surgery and noted in every 10 minutes. Patient was reversed with Neostigmine & Glycopyrolate and transferred to PACU for monitoring.

In Group S, Patients were placed in sitting position and under aseptic technique Inj. 0.5% Bupivacaine (hyperbaric) was given in L3-L4 intervertebral space using 25 G quincke spinal needle. After placing the patient on supine position, the head end of table in tilted down for few minutes until the desired level being obtained. Then cystoscopy and urethral catheterization was done by urologist in lithotomy position and patient made prone. HR, SPO2, SBP, DBP, MAP were monitored through-out the surgery, every two minutes for the first 10 minutes and then every 5 minutes for another 20 minutes and noted in every 10

minutes intervals. Patient was shifted to PACU after the procedure for monitoring. PCNL was done in both groups with fluoroscopy control to locate the stone and nephrostomy tube was placed in case of residual stones.

Besides this, in both groups, Anesthesia duration, Surgery duration, Recovery duration, Blood Loss, Analgesic demand & Blood transfusion if needed was recorded. Visual Analogue Scale was used for Pain severity and analgesic demand fulfilled accordingly.

Analgesic demand was fulfilled by Inj. Paracetamol 1gm & Inj. Morphine.

In postoperative period the following parameters was assessed viz. Nausea & Vomiting, Analgesic requirement, blood transfusion if required and later at the time of discharge from hospital patient's satisfaction & hospital stays noted.

Patient was shifted to ward in 2nd postoperative day and discharged after removal of nephrostomy tube.

Data analysis in this study was done with SPSS with data analyzed by chi-square test and student's t test and data taken as mean ± SD. p-value < 0.05 was considered significant.

Results

Out of 60 patients of ASA grade I between 20-60 years of age, of either sex posted for PCNL, randomly divided into two groups – Group G and Group S.

Table 1: Comparison of Patient's Characteristics:
We noted that there were no significant differences between two groups in terms of age, sex and weight. The demographic data are shown in Table 1.

PARAMETERS	Group G	Group S	P-value
Mean Age (years)	34.87 ± 9.95	38.03 ± 12.11	0.27
Male	16 (53.3%)	12(40%)	0.3
Female	14 (46.7%)	18(60%)	-

Weight (kg)		55.90 ± 7.12 6	52.20 ± 7.12	0.07
ASA	I	30	30	-
	II	0	0	-

Table 2: Comparison of stone sizes & Locations:
On comparing the Stone & its location as shown in the Table 2 regarding the numbers of stones and stones location, there was no significant when comparing between the two groups.

	Variables				
	Mean Stone size (mm)	Numbers of stones	Location of Stones		
			Pelvic stone	Calyceal stone	Staghorn stones
Group G	26.3 ± 6.6	3.4 ± 3.6	21	6	3
Group S	27.6 ± 5.8	3.8 ± 3.1	23	5	2
P-value	0.243	0.302	0.74	0.422	0.233

Table 3: Comparison of Anesthesia & Surgery duration, Recovery duration, Blood loss
In Table 3: Comparing the Anesthesia & Surgery duration & Recovery duration between two groups, general anesthesia groups had a more time required in terms of recovery of patients when compared with the spinal anesthesia groups and was statistically significant. Blood loss in case of general anesthesia groups was more than in spinal anesthesia groups and thus statistically significant. There were no significant differences in between the group for Anesthesia and Surgery duration.

Variables	Group G	Group S	P-value
Anesthesia Duration	78 ± 10	72 ± 8	0.144
Surgery Duration	70 ± 12	62 ± 14	0.122
Recovery Duration	85 ± 10	74 ± 10	0.007
Blood Loss	13	3	0.004

Table 4: Comparison of Post-Operative Outcomes
Table 4: In terms of Post operative outcomes, Analgesia demand was seen more in general

anesthesia group when compared with the spinal anesthesia group and statistically significant. Analgesic demand was fulfilled by Injection Paracetamol 1 gm & Injection Morphine.

Nausea & vomiting was seen in 2 patients among general anesthesia groups where as 1 patients had Nausea & Vomiting in spinal anesthesia groups. There was no significant difference in terms of Patient's satisfaction where compared in both groups.

Blood transfusion was done in 13 patients from general anesthesia groups and 3 patients in spinal anesthesia groups and was statistically significant.

Hospital stays was more in case of general anesthesia groups when compared with the spinal anesthesia groups and thus significant.

Variables	Group G	Group S	P- value
Analgesic demand (Post operative)	14.6 ± 2.4	8.2 ± 1.2	0.0001
Nausea & Vomiting	2	1	0.55
Patient Satisfaction	24	26	0.615
Blood Transfusion	13	3	0.004

Table 5: Intraoperative Mean Heart Rate compared between two groups

The Mean Heart rate comparison is shown in Table 5. When compared with the baseline, in both the groups there were significant difference in mean heart rate in 10 min, 20 min, 30 min, 40 min while there after were no significant difference between two groups.

Mean Heart rate	Group S	Group G	P value
Baseline	76.73 ± 15.74	79.80 ± 10.67	0.3
10 min	85.20 ± 15.24	95.23 ± 11.44	0.006
20 min	82.30 ± 13.92	90.83 ± 11.76	0.01
30 min	78.23 ± 12.17	85.20 ± 9.97	0.01
40 min	74.87 ± 13.45	83.87 ± 12.35	0.009
50 min	74.07 ± 13.37	75.87 ± 9.09	0.54

Table 6: Intraoperative mean MAP (mean arterial pressure) compared between two groups

The mean of Mean arterial pressure (MAP) measured during intra-operative period compared between two groups are shown in Table 6. There were no significant differences between the groups except in 10 and 20 minutes.

Mean MAP	Group S	Group G	P value
Baseline	92.70 ± 10.27	95.13 ± 11.04	0.38
10 min	90.23 ± 16.86	98.53 ± 17.29	0.06
20 min	79.93 ± 13.80	88.67 ± 14.31	0.01
30 min	76.13 ± 14.16	83.50 ± 15.19	0.057
40 min	76.53 ± 12.56	79.17 ± 14.11	0.44
50 min	85.87 ± 11.46	82.33 ± 15.89	0.32
60 min	84.27 ± 10.22	81.14 ± 13.14	0.26

Discussion

Anesthesia in PCNL plays an important role in determining the patient's quick recovery and thus hospital stay. In our study we have found that Spinal anesthesia in PCNL has more advantage as compared with general anesthesia in terms of hemodynamically stability, analgesic demand, recovery duration, Blood loss and Hospital stay.

S. Sraban Routray et al [7] who compared the surgical outcome and complications between spinal and general anesthesia undergoing PCNL and found that spinal anesthesia maintains better hemodynamic and haemostatic state, avoids general anesthetics complications, decreases the need of analgesics and duration of surgery. G. Movasseghi et al [8] compared Spinal with general anesthesia during percutaneous lithotomy and concluded that spinal is as effective and safe as GA and also under SA requirement of analgesics was less and showed hemodynamically stability during surgery and recovery period. This is same with our results where the need of analgesia was less in spinal group and also recovery time was less and hemodynamic stability was more in spinal groups.

B. Borzouei et al [9] found that spinal anesthesia is feasible, safe and well tolerated in management of patient with

renal stones, which also is our finding with spinal anesthesia group.

Kuzgunbay B, et al [10] studied 82 patients undergoing PCNL and compared general anesthesia with Spinal anesthesia and found no significant differences in two groups in terms of age, location of stone, operative time and hospital stays, which was also insignificant in our study except hospital stays in spinal anesthesia was less than in general anesthesia group.

Andreoni C, et al [11] studied impact of single dose of spinal analgesia on postoperative pain and recovery following PCNL, and found significant decrease in postoperative parenteral pain medication requirement and early ambulation and also found the decrease incidence of PONV, which was similar to our findings where spinal anesthesia group needed less amount of analgesic demand when compared with the general anesthesia groups.

Sung soo kim et al [12] studied and compared two groups and reported that post operative fever rates and hospital stays were greater in the general anesthesia group in compared with Spinal anesthesia group and this was common finding in our study where general anesthesia group required more hospital stay than spinal anesthesia group.

Mehrabi et al [13] studied 160 patients posted for PCNL in prone position and concluded that spinal anesthesia was an good alternative technique compared with general anesthesia and was similar in our findings.

Singh et al [14] studied and compared PCNL under general anesthesia and CSEA and found that CSEA was as effective and safe, and also found that the requirement of analgesia within first 24 hours was lesser in CSEA group with shorter hospital stays. Though our study was with spinal anesthesia but single shot Spinal anesthesia showed a similar beneficial

effect when compared with general anesthesia group.

Tangpaitoon T et al [15] studied and compared Spinal with Regional anesthesia undergoing PCNL in 50 patients and found that regional anesthesia was associated with greater patient satisfaction, lesser post-operative pain and lesser adverse effects.

Karacalar et al [16] compared spinal epidural block with general anesthesia and found that more patient satisfaction, less postoperative pain and lesser requirement of analgesia in spinal epidural group. Incidence of Vomiting, hypotension and bradycardia, there were no significant difference between two groups. Here the comparison was with epidural block and our study was with spinal anesthesia, despite this they showed more or less similar to our findings.

Therefore, on the basis of above studies and the results of above findings spinal anesthesia seems to be superior when compared with general anesthesia for performing the PCNL. In our study as the location of stones, sizes were more or less similar, duration of anesthesia and surgery were not significant in both groups. But, overall findings like less analgesics demand, faster recovery and less blood loss, patient's satisfaction and less hospital stays in spinal groups and hemodynamically stability with less blood transfusion showed spinal anesthesia as superior or equally beneficial in performing a PCNL.

Conclusion

Thus, we can conclude that Spinal Anesthesia during PCNL is more acceptable and stable in terms of hemodynamic stability, less blood loss, reduced analgesic demand, faster recovery which in turn improved the patient's quality of life with less hospital stay. Therefore, spinal anesthesia can be preferable choice for an anesthesiologists & urologists thereby

decreasing the complications of general anesthesia.

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Original Article

Monitoring of Ovarian Follicular Development and Ovulation with Transvaginal Sonography (TVS) in Infertile Women in Eastern Region of Nepal

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Abstract

Background

Ultrasonography is the first line imaging modality for evaluation of ovaries, monitoring ovarian follicular development and detecting ovulation in infertile women; thus plays a significant role in infertility management. This study was undertaken to evaluate the pattern of ovarian follicular growth and to predict and detect ovulation in infertile women by transvaginal sonography in eastern region of Nepal.

Material and Methods

Hospital based prospective cross-sectional study on 100 infertile patients referred for ultrasonographic monitoring of ovarian follicle was conducted over duration of 26 months. Serial transvaginal sonography of the patients was performed using standard procedure daily from day 10 of menstrual cycle till detection of ovulation. Identification of ovarian dominant follicle, monitoring of dominant follicle development and detection of ovulation was assessed in relation to the day of menstrual cycle.

Results

Increase in mean diameter of the dominant follicle was seen in serial ultrasound scan till ovulation, which occurred in all cases by day 16 of menstrual cycle. The average daily follicular growth rate \pm SD from day 10 of menstrual cycle till detection of ovulation was 2.2 ± 0.2 mm per day and the mean diameter \pm SD of dominant follicle on the day prior to ovulation was 21.4 ± 2.8 mm (range: 17.2 – 26.3 mm).

Conclusion

Transvaginal sonography is an excellent method for monitoring of ovarian follicular development and shows a linear increase in mean diameter of dominant follicle from day 10 of menstrual cycle till detection of ovulation.

Key Words: *Dominant follicle, Infertility, Transvaginal sonography (TVS)s*

Introduction

Infertility is inability of a sexually active couple to achieve pregnancy even after one year of unprotected coitus [1] and 10-15% of reproductive age couples come across this situation. Of the various causes of

female infertility, disorders of ovulation account for about 20-40% and are among the most easily diagnosed and treatable causes of infertility [2].

Imaging plays an important role in evaluation of infertile women and

ultrasonography is the first line investigation in these patients [3,4]. Ultrasound is readily available, safe (radiation free), easy to use, noninvasive and easily repeatable imaging modality for evaluation of ovaries and monitoring ovarian follicular development in infertile women and thus an essential and integral part of both the diagnostic and therapeutic steps in infertility management [4,5]. Even though both transvaginal and transabdominal approach can be used to visualize ovaries, monitor ovarian follicular development and detect ovulation; transvaginal approach allows more frequent and better detection and visualization of ovaries and ovarian follicles, and a serial ultrasonographic monitoring provides a reliable measure of follicular growth and detection of ovulation [6,7]. Ultrasonographic documentation of changes in ovaries during normal cycles and assisted reproductive technology has a great significance and role in infertility treatment which includes detection of ovarian follicles and development of dominant follicle, timing administration and adjustment of ovarian stimulatory drugs, document ovulation, provide guidance during oocyte retrieval and predict and detect ovarian hyperstimulation syndrome [5,8].

This study was undertaken to evaluate the pattern of ovarian follicular growth and to predict and detect ovulation in infertile women seeking treatment in teaching hospital in eastern part of Nepal.

Materials and Methods

Prospective cross-sectional study on 100 consecutive patients with infertility referred for ultrasonographic monitoring of ovarian follicle to Department of Radiodiagnosis and Imaging of Nobel Medical College Teaching Hospital and Research Center, Biratnagar was conducted over a period of 26 months from March 2014 to April 2016. Patients with irregular menstrual

cycles and patients already on ovulation induction drugs were excluded from the study.

The patients were explained about the procedure of transvaginal sonography and informed consent was obtained. Demographic data such as age and duration of marriage were inquired and recorded. Serial transvaginal sonography of the patients was performed in the presence of female attendant using standard procedure daily from day 10 of menstrual cycle till detection of ovulation. The day of ovulation was defined as the day when the ultrasound examination showed disappearance or regression of size of dominant follicle. Following features were assessed and recorded:

- The presence of follicles within the ovary and average dimension of follicles.
- Identification of dominant follicle and side of ovary in which it was seen.
- Changes in dominant follicle (size) on serial ultrasound scan.
- Detection and documentation of ovulation with associated sonographic signs of ovulation such as sudden disappearance of follicle or regression of size, irregularity of margins, echogenic texture within the follicle and fluid in cul-de-sac.

Statistical Analysis

Statistical analysis was performed using SPSS software.

Results

Total of 100 patients referred for follicular monitoring were examined. The age range of the patients was between 19 – 43 years with a mean age of 29.1 years (Table 1). Average duration of marriage being 6.1 years (range 2 – 17 years) with 43 % of patients being married for less than 5 years, 41 % married for between 5 – 10 years and 16 % married for more than 10 years (Table 2).

Table 1: Age Distribution

Age group (years)	Frequency (n=100)	Percentage
15-20	2	2%
21-25	11	11%
26-30	40	40%
31-35	31	31%
36-40	13	13%
41-45	3	3%

Table 2: Marriage Duration

Duration (years)	Frequency (n=100)	Percentage
<5	43	43%
5-10	41	41%
>10	16	16%

Dominant follicle was seen in right ovary in 54 (54 %) patients, whereas in 46 (46 %) patients dominant follicle was noted in left ovary.

Increase in mean diameter of the dominant follicle was seen in serial ultrasound scan till ovulation, which occurred in all cases by day 16 of menstrual cycle.

Ovulation was observed on 14th, 15th and 16th day of menstrual cycle in 24 (24 %), 40 (40 %) and 36 (36 %) patients respectively. The mean diameter \pm SD of dominant follicle on 10th, 11th, 12th, 13th, 14th, and 15th day of menstrual cycle were 11.2 \pm 1.3 mm (range: 9.4 – 13.7 mm), 13.4 \pm 1.4 mm (range: 11.8 – 15.7 mm), 16.0 \pm 1.2 mm (range: 14.1 – 18.0 mm), 18.1 \pm 1.6 mm (range: 16.2 – 20.9 mm), 20.1 \pm 1.8 mm (range: 18.2 – 24.3 mm) and 22.2 \pm 1.8 mm (range: 20.2 – 26.3 mm) respectively. (Table 3).

Table 3: Mean diameter of Dominant follicle

Day of Menstrual cycle	10	11	12	13	14	15
Mean Diameter \pm SD (mm)	11.2 \pm 1.3	13.4 \pm 1.4	16.0 \pm 1.2	18.1 \pm 1.6	20.1 \pm 1.8	22.2 \pm 1.8

The average daily follicular growth rate \pm SD from day 10 of menstrual cycle till detection of ovulation was 2.2 \pm 0.2 mm per day and the mean diameter \pm SD of dominant follicle on the day prior to ovulation was 21.4 \pm 2.8 mm with a range of 17.2 – 26.3 mm.

Sudden disappearance / regression of size of dominant follicle as a sign of ovulation was seen in all cases with irregular margin observed in 91 % of cases. Echogenic texture within the follicle was seen in 86 % of the cases. Whereas in 42 % of cases free fluid was detected in cul-de-sac immediately after ovulation.



Figure 1: Dominant follicle in right ovary on transvaginal sonography performed on day 14 of menstrual cycle (mean diameter: 23.9 mm)



Figure 2: Involution of dominant follicle with increase internal echoes on transvaginal sonography performed on day 15 of menstrual cycle.



Figure 3: Free fluid in cul-de-sac after ovulation.

Discussion

Infertility is not only the problem of Western countries, but also of developing countries [9] and is overly associated with sentiment and misinformation [5]. Ultrasound is an investigation of choice in infertile women [4] for evaluation of ovaries and monitoring ovarian follicular development.

Majority of patients (40 %) in this study belonged to age group of 26 – 30 years and with 43.0 % of the infertile women in this study were married for less than 5 years. This early seeking for infertility treatment could be due to associated stigma with infertility in our society and couples increased awareness regarding available treatment facilities and importance of early detection and treatment of underlying causes of infertility.

Linear increase in mean diameter \pm SD of dominant follicle by 2.2 ± 0.2 mm per day was seen from day 10 of menstrual cycle till detection of ovulation in this study with the mean diameter \pm SD of dominant follicle on the day prior to ovulation being 21.4 ± 2.8 mm (range 17.2 – 26.3 mm), which was consistent and comparable with other studies [10-16].

Ojengbede OA et al in their study of 39 spontaneous cycles in 34 women (22

infertile and 12 normal volunteers) reported maximum mean follicular diameter prior to ovulation of 21.0 mm with a maximum mean follicular diameter prior to ovulation in infertile women to be 21.4 mm (range 15 – 28 mm) [10]. In a study by Lenz S follicles reached a maximum mean diameter of 20.5 mm with a range of 16 – 25 mm and average daily follicular growth rate of 2.2 mm per day [11]. Follicular growth by 2 - 3 mm a day reaching a mean diameter of about 20 – 24 mm by the time of ovulation was seen in study of Hackeloer BJ et al [12]. According to Sengoku K et al the mean follicle diameter in 28 infertile patients (for 48 cycles) measured the day before ovulation was 22.4 mm with the range of 16 – 27 mm [13]. In a study conducted by Kerin J, day to day preovular growth of follicle was linear with the range of the final diameter of ovarian follicle prior to ovulation to be 17 – 26 mm [14]. According to Bakos et al at ovulation the dominant follicle had a mean diameter of 21.4 mm with a range of 17.4 – 27.0 mm [15]. In a study carried by H M Behre et al on 53 women of age group 18 – 39 years for a total of 150 cycles, the mean follicular diameter on the day before ovulation was 21.5 mm [16]. However, in a study by Hata T et al in 21 infertile Japanese women during 37 menstrual cycles, the maximum mean diameter prior to ovulation was 23.3 mm [17] which was slightly higher than this study.

In the present study, sudden disappearance / regression of size of dominant follicle as a sign of ovulation was seen in all cases. However, in studies of Guermandi E et al [18] and Luciano AA et al [19] in infertile women, rupture of the dominant follicle was evidenced in 96 % and 94 % of cycles respectively. Echogenic texture within the ruptured dominant follicle was seen in 86 % of cases, which was comparable with the study of Ojengbede

OA et al [10] who found the changes in shape and / or size of follicle mostly associated with increased internal echoes as the indices of ovulation in 84.7 % cases. Free fluid in cul-de-sac immediately after ovulation was detected in 42 % of cases which is comparable to the study of Sengoku K et al [20] in which free fluid in cul-de-sac was demonstrated in 41.8 % of cases. However, in a study of Davis JA et al [21] free fluid in cul-de-sac was detected in 26 % of cases in the period immediately after ovulation.

Conclusion

Transvaginal sonography is an excellent imaging investigation for identification of ovarian dominant follicle and a serial ultrasonographic monitoring provides a reliable measure of follicular growth and detection of ovulation, hence have a significant role in infertility management. Linear increase in mean diameter \pm SD of dominant follicle by 2.2 ± 0.2 mm per day was seen from day 10 of menstrual cycle till detection of ovulation with the mean diameter \pm SD of dominant follicle on the day prior to ovulation being 21.4 ± 2.8 mm (range: 17.2 – 26.3 mm). Hence prediction of ovulation depending upon the size of dominant follicle alone may not be accurate due to wide range of mean follicular diameter prior to ovulation; however, infertility management procedures can be carried out when the size of dominant follicle reaches in the range of presumptive ovulation.

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Original Article

Comparative Evaluation between Local and Spinal Anaesthesia for Inguinal Mesh Hernioplasty in Elderly Patients with Limited Cardiac Reserve.

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Abstract

Background

The choice of anaesthesia technique, based on its advantages and disadvantages in elderly patients with limited cardiac reserve will be influenced by the patient's comorbid diseases. The aim of the study was to compare the effects of spinal anaesthesia and local anaesthesia in elderly patients with limited cardiac reserve for inguinal mesh hernioplasty.

Material and Methods

In the present study 60 male patients between the ages of 65 to 92 with limited cardiac reserve, reported for mesh hernioplasty were equally divided in two groups. One group received spinal anaesthesia (SA) and the other group received local anaesthesia with nerve block (LA). Effectiveness and complications of both the group were evaluated.

Results

All patients had comorbid cardiac diseases with limited cardiac reserve along with hernia. Perioperative and postoperative complications were significantly more in SA group. All the surgeons and patients were satisfied with the operating conditions.

Conclusion

Nerve block anaesthesia with skin infiltration for inguinal mesh hernioplasty in elderly patients with limited cardiac reserve is recommended, as it is safe, patient friendly with less postoperative complications.

Key Words: *Cardiac disease, Elderly, Inguinal hernia, Local nerve block anaesthesia, Mesh repair, Spinal anesthesia.*

Introduction

Hernia is a Latin word that means rupture of a portion of a structure [1]. It is an abnormal protrusion of an organ or part of an organ or other structure through the wall of a cavity normally containing it. Till date 87 various types of hernias have been described [2]. Amongst all these right indirect inguinal hernia is the commonest and 80% to 90% are male patients [3]. The

aim of treatment of inguinal hernia is strengthening the abdominal wall by surgical repair as muscle weakness plays a major role in the etiology. Various techniques have been adopted viz, Bassini's repair, darned repair, shouldice's repair and so on [4,5]. But polypropylene mesh repair is very popular to strengthen the abdominal wall [6,7]. A large number of elderly patients with hernia also suffer from co

existing cardiac diseases, which lead to reduced cardiac reserve. Apparently these cardiac diseases may be stable in his day-to-day life, but may manifest as life threatening during surgery [8]. Myocardial ischaemia may occur in upto 25% of these cases whereas 1-3% cases may develop myocardial infarction during surgery [9]. Goal of hernia surgeries and anaesthesia in such problematic elderly patients should be to reduce recurrence, the most reliable and safe anaesthesia which is acceptable to patients and surgeons, less postoperative complications, cost, less hospital stay and quick return to normal life [4, 10]. Moreover, today anaesthesia technique should be customized according to the experience of anaesthesiologists. The concept of 'tailored surgery' for hernia repair has been well stressed in the recent guidelines of the "European hernia society" published in "hernia" in 2009, which recommends to take advantages of local anaesthesia for hernia repair. This is a grade A recommendation with high scientific impact [11]. Today the surgical and anaesthesiology groups of the world have welcomed these recommendations. But still it could not gain the momentum. So the purpose of the present study was to compare spinal with local anaesthesia with nerve block skin infiltration for mesh repair of inguinal hernia in elderly patients with limited cardiac reserve.

Materials and Methods

After obtaining approval from the hospital ethical committee 60 male patients in the age group of 65-92 who reported to Nobel Medical College Teaching Hospital for inguinal hernia repair during the period April 2015 to April 2016 with limited cardiac reserve due to some cardiac ailment, as evident clinically during preanaesthetic check-up (PAC) by "Match stick test" and "Breath-holding test" and willing to participate in the study were randomly and equally divided into two groups viz spinal

anaesthesia (SA group) and local anaesthesia with nerve block (LA group) by using sealed envelope technique. Morbidly obese patients, incarcerated or obstructed or strangulated hernias, hernia with hydrocele, recurrent hernia, bilateral hernia, sensitivity to local anaesthetics and patients with bleeding disorders or on anticoagulants were excluded from the study.

All the patients were thoroughly examined and investigated at the preanaesthetic clinic. CBC, blood sugar, renal and cardiac profile, chest X-ray, ECG, and trans thoracic echocardiography were done. The patients who had positive "Matchstick test" and "Breath-holding test" of <20s were subjected to PFT, TMT or stress TMT. An Ejection fraction <35%, a positive TMT or stress TMT indicated a reduction of cardiac reserve. Patients with positive coronary angiography were excluded from the study. All the medications were continued but aspirin was stopped 7 days before surgery. On the previous evening of operation and 2 hours prior to surgery all the patients received tab. lorazepam 2 mg and tab. ranitidine 150 mg orally.

On arrival at the OR every patient was put on standard noninvasive monitor to record SPO₂, HR, SBP, DBP, MAP. An IV access with 18-gauge cannula was established to start infusion of ringer lactate /normal saline at the rate of 6 ml/kg of body weight 20 minutes before anaesthesia. O₂ was administered throughout the surgery and any significant happenings or abnormality was immediately documented and corrected. All the blocks were performed under strict aseptic conditions.

Technique of spinal anaesthesia

Lumbar puncture for all the patients in spinal anaesthesia group were done in sitting position via a midline approach with a 25 G quincke needle. After a successful dural puncture with free flow of CSF, spinal anaesthesia was performed with 15mg of

0.5% heavy bupivacaine and immediately patient was put on supine position.

Technique of nerve block

In local anaesthesia group, all the nerve blocks were performed with 1% preservative free lignocaine hydrochloride (loxicaid) mixed with freshly prepared adrenaline to make strength of 1:200000. The nerve supply of the inguinal region is from the last two thoracic and the first two lumbar nerves via the iliohypogastric, the ilioinguinal and the genital branch of genitofemoral nerves. In addition, a few nerve twigs overlap from the opposite side over the spine of the pubis.

For successful block Macintosh's technique was followed, 3 wheals were raised

- 1) 2cm medial to the anterior superior iliac spine
- 2) Over the spine of the pubis
- 3) Half inch above the midpoint of the inguinal ligament which corresponds to the deep inguinal ring
- 4) At the base of the scrotum to block the spermatic cord.

Through wheal one a 22/23G large needle (3" to 3 ½ ") is introduced vertically backwards until it is felt to pierce the aponeurosis of the external oblique with a slight click. After aspiration, 15 ml of 1% solution is injected so that both the ilioinguinal and iliohypogastric nerves are surrounded and blocked. It is safe at this point, as a needle-inserted perpendicular will not pierce the peritoneum. Five ml solution is also deposited in all layers in the small area of tissue between the wheal and the anterior superior iliac spine.

Through wheal 2 about 5 ml of solution is deposited in the intradermal and subcutaneous layers in the direction of the umbilicus. This blocks the nerve twigs from the opposite side. Through wheal 3 a 22G, 2" hypodermic needle is inserted perpendicular to the skin until it pierces the aponeurosis of the external oblique. At this level another 10 ml of 1% solution was

injected to block the genital branch of the genitofemoral nerve. Through wheal 4, five ml of 1% solution was injected in the spermatic cord after holding it firmly between the thumb and index finger of the left hand, taking extreme precaution not to inject the drug in the pampiniformplexus or injure the vas deferens.

Lastly, using a 25 G, quincke type spinal needle an intradermal and subcutaneous infiltration with 5ml of 0.5% solution was administered to produce perfect analgesia keeping the total dose of lignocaine with adrenaline less than 500mg.

If during dissection of the neck of sac pain was experienced, 2 ml of 1% solution was reserved for injection in the extra peritoneal pad of fat at the neck of the sac. But no patient needed this. All the patients were sedated with midazolam 2mg IV and fentanyl 50mcg IV.

Three experienced surgeons and two anaesthesiologists were involved in the whole research. Surgeons were requested to perform sharp dissection, not to pull the spermatic cord and sac harshly, to be gentle with the gut and omentum, when these were the contents of the sac and to cauterize even small oozes as LA drug was mixed with adrenaline.

Approximate size mesh was fixed with coarse interrupted sutures overlapping the lateral tail of the mesh to provide a snug fit around the cord. After surgery the patients were transferred to post anaesthesia care unit where patients were monitored for pain, nausea, vomiting, hypotension, wound hematoma and urinary retention.

During and after surgery, surgeons and all the patients were asked to express their opinion and satisfaction level about the whole procedure.

Results

In the present study we observed and analyzed the most relevant and important preoperative, perioperative and postoperative data of all the patients and

clubbed them in table 1 to table 6 for comparative evaluation between the two groups.

Table 1: Primary data of the study

There were no statistical significant differences (p values) in age and location of hernia. But there is a significant statistical difference between the 2 groups regarding the type of hernia. (Table 1)

S. N	Comorbids	SA group	LA group	TOTAL
1	H/o Coronary artery disease	4	10	14
2	Angina pectoris (stable) with ECG changes	3	6	9
3	History of Myocardial Infarction	2	4	6
4	Coronary artery disease with DM /stroke/syncope/COPD	2	4	6
5	Mild (well compensated) valvular heart disease	7	1	8
6	Conduction defects 1 st degree heart block	5	1	6
7	Ectopics	5	1	6
8	Atrial fibrillation with h/o syncope	2	3	5

Table 2: Comorbid diseases

Factors	SA group	LA group	Independent T test	pValue
Age (mean \pm SD)	73.86 \pm 6.274	73.13 \pm 6.230	0.45469 (58)	0.651
Sex	M	M		
Details of hernia	SA group	LA group	Chi square	pValue
Site			0.0733	0.787
Right	20	19		
Left	10	11		
Type			32.9	<0.001
Direct	28	6		
Indirect	2	24		

Table 3: Comorbid disease according to ASA classification

All the 60 patients in the present study had some comorbid disease (Table 2). The total number of patients in ASA III and ASA IV were much higher (27) in the LA group than SA group (13), which is statistically significant. (Table 3)

ASA	SA group	LA group	Chi square	pValue
II	17	3	14.7	<0.001
III and IV	13	27		

TABLE 4: Perioperative complications

One of the most striking features of the study was statistically significant increase in the incidence of perioperative complications in SA group. (Table 4).

Factors	SA group	LA group	chi square	p value
Hypotension			30.9	<0.001
Mild >upto 20mmHg	16	8		
μ Moderate upto 20-40mmHg	14	4		
μ Severe <40mmHg	8	2		
Bradycardia	23	6		
Tachycardia	12	10		
Arrhythmia	16	2		
Cardiovascular collapse	4	0		
Respiratory depression	2	6		
Hypertension	3	8		
Nausea	16	4		
Vomiting	8	0		
Surgery time	50-65 mins	60-75 mins		

Only 2 patients in LA group had arrhythmia (PSVT, 1st degree heart block) whereas 16 patients in SA group had arrhythmia (ventricular ectopics, 1st degree heart block, transient ST depression)

There was not much difference in the operating time between the two groups.

TABLE 5: Intraoperative pain (VAS score) and operating condition (surgeons opinion)

Factors	SA group	LA group	chi square	p value
Pain μ 1-2-nil μ 3-4-mild discomfort μ 5-7-moderate pain μ 8-10-severe pain	25 2 1 2	18 6 5 1	6.14	0.105
Operating condition (surgeons opinion) μ Excellent μ Good μ Satisfactory μ Unsatisfactory	15 10 1 4	10 15 2 3	2.48	0.48
Patients opinion (scale of 5) μ Absolutely satisfied μ Very satisfied Moderately satisfied μ Satisfied Disappointed	13 7 6 2 2	5 10 8 4 3	5.24	0.264
Sedation and analgesics Midazolam Fentanyl	1-2 mg 30-50 mcg	2-2.5mg g 50-150mcg		

Mild discomfort or no pain was reported by maximum number of patients in both the groups and this was statistically insignificant. (Table 5)

There were 3 failures in LA group. Though the requirement of midazolam and fentanyl were more in LA group but overall assessment of the satisfaction level in both the groups shows no statistical difference. Satisfaction level as per patient’s opinion, show that more than 90% in both the groups were satisfied with the surgical and anaesthetic procedures and there is no statistical difference between the groups.

TABLE 6: Early post op complications and side effects

Factors	SA group	LA group	chi square	pValue
Postop complications · Hypotension · Urinary retention · Local hematoma · Infection · Nausea/vomiting · Itching	22 20 3 1 15 2	5 5 12 3 5 14	37.9	<0.001
Hospital stay Mean ±SD (days)	4 ± 1.082 days	2 ± 0.74 days		

Statistically significant more number of patients in the SA group had postoperative complications. But the incidences of itching and local hematoma were much higher in LA group. LA group also had less hospital stay. (Table 6)

Discussion

Any type of protrusion of abdominal cavity contents due to the weakness of the abdominal wall in the inguinal region is called inguinal hernia [12]. Curative treatment of this type of pathology is exclusively surgical. Since Bassini’s period (1844-1924) various methods of hernia repair have evolved for better results. All researchers agree that the ideal method of repair is one that causes minimal discomfort to the patient, technically simple, should have low rate of complications and recurrence [13,14]. So now everybody recommends use of prosthetic mesh, which allows tension free repair of hernia [15]. Repair of hernias are generally performed under general anaesthesia, regional anaesthesia (spinal or epidural) with their inherent risks. This risk

is more in cases of elderly patients where the patients had associated cardiac, pulmonary or other illness [16,17]. Another alternative technique of anaesthesia for hernia repair is local anaesthesia that has minimal side effects or perioperative and early postoperative complications. Several studies [18-20] like the present study and the grade A recommendation of the "European Hernia Society" in the year 2009 have shown that local anaesthesia provide best clinical, economical benefits to the patients as well as it is safer and patient friendly than other techniques.

Local anaesthesia again maybe stepwise infiltration anaesthesia with moderate to deep level of sedation or analgesics. But deep sedation sometimes may produce problems in very elderly patients with cardiorespiratory or other comorbid diseases. International literatures, current evidences as well as general recommendations of the "European hernia society" suggests the use of ilioinguinal nerve blocks with stepwise local infiltration anaesthesia [7,11,21]. But the nerve supply of the inguinal region is from last two thoracic and first two lumbar via ilioinguinal, iliohypogastric and genital branch of genitofemoral nerves. In addition, some overlapping fibres from the opposite side also innervates the small area on the medial part of inguinal region. So the present study was designed to block these three nerves and the overlapping fibres from the opposite sides separately to have a better quality of anaesthesia. As all these patients in the present study had limited cardiac reserve it was planned to use preservative free lignocaine and to add adrenaline to it to make the strength 1:200000 as this type of solution is not available in the world market. We used this type of solution for 3 reasons. 1) Loxicard is used for treating arrhythmias so may have some benefit in patients with limited cardiac reserve. 2) Less toxicity as it does

not contain preservative 3) Expert opinion-our experience to use this type of solution in such cases for more than 3 decades with good results. But "PubMed" search did not reveal any report of this type. The present study show that for inguinal hernia repair, LA with nerve block along with skin infiltration with preservative free lignocaine with adrenaline; 1:200000 offered several advantages over spinal anaesthesia. It is also safe and patient friendly and surgeons graded the operating condition to be good or excellent. Moreover, added advantage is it does not have the specific side effects and complications of spinal anaesthesia, like PDPH, spinal hematoma, permanent neurological sequel and transient radiculitis. So the current recommendation of several researchers like T Callesen, H Kehlet, EY Akcaboy, ZN Akcaboy[22,23] and the "European hernia Society" (grade A 2009) is to use LA for repair of inguinal hernia if there is no contraindication. But still today spinal and lumbar epidural anaesthesia are very popular with their inherent risks particularly in elderly with comorbid diseases for hernia repair because it is easier and quicker to administer and anaesthesiologists are well trained. The cardiovascular effect gets augmented after SA because the chemical sympathectomy always extends 2-6 dermatomes above the sensory level [24]. Patients of coronary artery diseases have fixed diameter vessel, so hypotension leads to decreased O₂ delivery, less cardiac output and a further drop of blood pressure. It is problematic to administer rapid intravenous fluids in these cardiac patients, so vasopressor remain the only choice. Moreover, systemic vascular resistance in elderly cardiac patients may decrease to 25% of normal, making them more vulnerable to hypotension and resistant to treatment [24]. Because of all these effects most of the authors traditionally recommend to avoid spinal

anaesthesia particularly in elderly patients with ischaemic and other heart diseases. All these problems do not occur in nerve block anaesthesia [5]. However, despite the advantages of LA this technique could not gain the wide scale popularity of the surgeons and anaesthesiologists [25,26] outside dedicated hernia centers [27].

In reality many other factors play a part like tradition, surgeons preference, time taking particularly for the inexperienced anaesthesiologists, inadequate training, fear of failure of the block. Many anaesthesiologists finish their training without much exposure in this field. So in practice they feel uncertain about the block and instead use other techniques like SA, epidural, GA and thereby expose their patients to much more hazards[28]. But a well-trained anaesthesiologist should be exposed to all types of anaesthesia during training so that he or she can tailor the safe anaesthetic need of his patient, which is the basic concept, and talk of today's "customized" "tailored surgery".

Conclusion

"In many cases local anaesthesia means least strain to the patients" T.Gordh (1907-2010)

The present study substantiates this old saying of Gordh and concludes that between spinal and local anaesthesia for inguinal mesh hernioplasty for elderly patients with limited cardiac reserve, local anaesthesia with nerve block along with skin infiltration with preservative free lignocaine with adrenaline; 1:200000 should be considered and practiced as it is better, safer and an effective choice. Properly administered by experienced anaesthesiologists nerve block for mesh hernioplasty is patient friendly with less incidence of anaesthesia related complications, hospital stay, cost and offers a hemodynamically stable patient. This technique needs more intense training to residents and trainees as -

"Bright is the ring of words; when the right man rings them up"

- Robert Louis Stevenson (1850-1894)

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Original Article

Socioeconomic and Reproductive Factors Related to Low Birth Weight Babies

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Abstract

Background

Birth weight is a major determinant of morbidity, mortality and disability in neonates and children. Low birth weight (LBW) is associated with high morbidity, mortality and lifelong consequences. Hence, it is prudent to identify the risk factors causing LBW neonates and manage them promptly.

Material and Methods

This study was conducted at Nobel Medical College Teaching Hospital (P.) Ltd. which included term singleton neonates born via normal vaginal route without gross congenital anomalies and sickness at birth. Birth weight of neonate and mother's socioeconomic and reproductive history was taken within 24 hrs of birth.

Results

There were 429 infants with birth weight ranging from 1500 gm to 4000 gm with mean birth weight of 2815.84 gm. The incidence of LBW was 21.9% (n=105). Body Mass Index at first Ante Natal Visit (ANV), mother's age, occupation, smoking, history of abortion and last pregnancy interval were the most important associated variables for LBW.

Conclusion

Better nutrition during pregnancy, better education of mothers, avoidance of smoking, regular ANV and early commencement of ANV, increasing birth spacing and iron and folic acid supplementation will decrease the incidence of LBW and its consequences.

Key Words: *Antenatal visits, Low birthweight (LBW), Neonatal mortality*

Introduction

The first weight of newly born baby taken after birth is the birth weight. For those born alive, measurement of the birthweight should be done within the first hour of life, before the baby loses significant weight in the immediate postnatal period. In 1976, the 29th World Health Assembly agreed on the following definition of low birth weight that "Low birth weight is a weight at birth

of less than 2,500g (up to and including 2499) irrespective of gestational age".

Birth weight is an important indicator of child survival. Appropriate and timely care of a new born especially if he/she is born with low birth weight is important but this is difficult in developing countries since most of the deliveries are conducted at home where adequate facilities to weigh a newborn do not exist [1]. One of the most dependable and sensitive predictors

of community health is the birth weight [2]. It is estimated that 18 million babies are born with low birth weight and half of them are born in south Asia [3]. The estimates of prevalence of LBW in Nepal have ranged from 14% in community based studies to 32% in hospital based ones, overall being 27%.

The babies born with low birth weight have almost 40 folds more chances of dying during the neonatal period when compared to those born with normal birth weights. Two third of the neonatal deaths accounts to babies with birthweight ≤ 2.5 kgs and about half of the deaths accounts to those weighing ≤ 1.5 kgs [3]. In most of the countries both biological and service related factors have a significant impact on birth weight. Of these factors, teen pregnancy, poor antenatal care and maternal under nutrition, education may play pivotal roles in causing LBW. An association between lack of prenatal care and adverse outcomes of pregnancy such as perinatal and maternal mortalities, preemies and LBW have been shown by many studies.

This study was conducted to identify the mothers socioeconomic and reproductive factors which are directly and indirectly related to the LBW babies.

Material and Methods

This cross-sectional observational study was conducted at Nobel Medical College Teaching Hospital Pvt. Ltd. Hospital, Biratnagar, Nepal from June 2013 to July 2013 and the principal focus of this study was to ascertain the significant determinants for LBW. This study included 479 term singleton neonate born via normal vaginal route without gross congenital anomalies and sickness at birth.

The detailed socioeconomic and obstetric history was obtained from mother and father (if present). Information gathered were: Hospital number, 1st day of LMP, weight of mother at the time of first antenatal visit (taken from the ANC card),

mother's height, sex of the child (in grams), date of delivery, gravid of mother, and para, mother's age, resident of mother, mother's education and occupation, monthly income, number of family members, type of family she is living with, religion, smoking habit, alcohol intake or not, dietary habit, any death of previous child, previous abortion or still birth, number of antenatal visits, time of first antenatal visit, the last pregnancy she had and iron and folic acid supplementation. Weighing of all the neonates was done before 24hrs of birth by an electronic weighing scale manufactured by Phoenix Company (in India with collaboration), which had sensitivity up to 10 grams.

Results

There were 236(49.3%) male and 243(50.7%) female infants. The birth weight ranged from minimum 1500 gm to maximum of 4000 gm with mean birth weight of 2815.84 gm. The incidence of LBW was 21.9% (n=105). Among different possible risk factors studied and analyzed, female sex of new born, body mass index of mother at first antenatal visit, age of the mother, residence, education, income, occupation, income, family type and number of family members, smoking habit, history of previous abortion, number of antenatal visits, time of commencement of first antenatal visit, interval between the current and previous pregnancy and supplementation with iron and folic acid during pregnancy were significantly associated with the incidence of LBW. Alcohol intake by mother, dietary habit of mother, history of death of previous child was found to be statistically insignificant. After doing adjustments for the confounding variables by the logistic regression analysis, BMI at first antenatal visit, mother's age, occupation, smoking, history of abortion and last pregnancy interval were the most important associated variables for LBW.

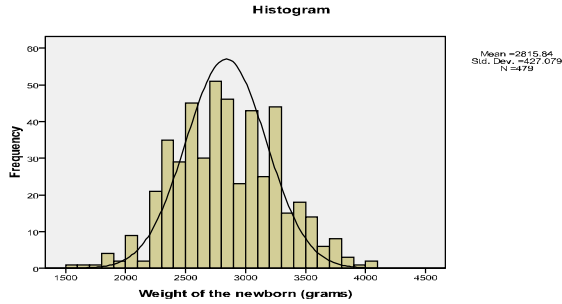


Table 1: relationship of BMI of mother with LBW

	Weight of the newborn (grams)				p-value
	Normal		LBW		
	N	%	N	%	
< 18.00	0	.0%	25	100.0%	<0.001
18-24.99	370	83.0%	76	17.0%	
Total	370	78.6%	101	21.4%	

Table 2: relationship of sex of newborn with LBW

	Weight of the newborn (grams)				p-value
	Normal		LBW		
	N	%	N	%	
Male	194	82.2%	42	17.8%	0.032
Female	180	74.1%	63	25.9%	
Total	374	78.1%	105	21.9%	

Table 3: relationship of gravidity of mother with LBW

	Weight of the newborn (grams)				p-value
	Normal		LBW		
	N	%	N	%	
1	186	75.0%	62	25.0%	--
2	151	86.8%	23	13.2%	
3	32	69.6%	14	30.4%	
4	5	50.0%	5	50.0%	
5	0	.0%	1	100.0%	
Total	374	78.1%	105	21.9%	

Table 4: Relationship of Smoking with LBW.

	Weight of the newborn (grams)				p-value
	Normal		LBW		
	N	%	N	%	
Yes	31	58.5%	22	41.5%	<0.001
No	343	80.5%	83	19.5%	
Total	374	78.1%	105	21.9%	

Discussion

Birth weight, the weight of a neonate taken soon after birth, is the single most important indicator of neonatal outcome as

well as overall health status later in life. In most of the third world countries including developing country like ours the incidence of low birth weight is high [4]. The problem of low birth weight needs to be addressed on priority basis as the children are the future the country. Low birth weight neonates need special care since they have increased risk of mortality and long term morbidity [5].

There were 236(49.3%) male and 243(50.7%) female in this study and male to female ratio was 0.99:1 and the rate of LBW was 21.9%. Birth weight of all term neonate ranged from minimum 1500 gm to maximum of 4000 gm with mean birth weight of 2815.84 gm with standard deviation 427.079 gm. In this study most of the women were between 20-29 years of age (71.4%) with 19.2% from age group of < 19 years and 13.4% of women above 30 years. In this study BMI of mother was significantly associated with the birth weight of newborn (p value <0.001) where none of the mother BMI <18 had normal birth weight infants. Female sex was significantly associated with LBW (p value =0.032). The age of the mother was significantly associated birth weight of the neonate (p value <0.001).

Mothers with no education and primary level of education had more child with LBW as compared to babies born to mother with secondary or higher level of education and the relation was significant (p vale < 0.001). Most of the LBW were form the mothers who were housewife by occupation as compared to job holder mothers (private or government). Association between maternal income and its effect on birth weight was also studied and direct relationship was observed as most of the LBW were from the mothers with low income group as compared with high income group with p value < 0.001.

In family members of 2 the incidence of LBW was 19.6% while in family members

≥ 5 incidence of LBW was 37.8% which was very significant (p value < 0.001) and incidence of LBW was 17.6% in nuclear family and 35.3% in mothers from joint family which was also significant (p value < 0.001). Whether maternal smoking during pregnancy affects the birth weight of neonate or not was also tried to study and the relationship was found statistically significant (p value < 0.001) that incidence of LBW was higher among smoker mother as compared to non smoker mothers (41.5% Vs 21.9% respectively). In this study there was significant relation between the history of previous abortion and the LBW of subsequent newborn (p value < 0.001).

Those mothers received 4 or more antenatal care gave birth to higher birth weight in comparison to mothers who received 2 or less antenatal care visit (13.3% Vs 54.5% respectively) with p value < 0.001 . The incidence of low birth weight was higher in the mothers with interval < 24 months as compared with mothers with interval > 24 months (34% Vs 6% respectively). The relationship between the intake of iron and folic acid during pregnancy and its effect on birth

weight was studied which showed the significant relationship with p value < 0.001 .

Conclusion

So from this study we conclude and recommend that better nutrition during pregnancy, better education of mothers, avoidance of smoking, taking regular ANC visit and commencement of ANC visit from the first trimester of pregnancy, increasing the birth spacing and taking iron and folic acid regularly will decrease the incidence of LBW and morbidity and mortality from LBW.

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Original Article

Characterisation and Isolation of Candida Species from ICU Patients in Nobel Medical College Teaching Hospital, Biratnagar

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Abstract

Background

Fungi have emerged as major causes of human diseases. Intensive Care Units (ICU), harbor almost all the risk factors for opportunistic fungal infections. Among these, Candida infections are very common with recent trends being rise in the non-Candida albicans (NCA) species along with an increase in resistance of these species to antifungal drugs. Increment in invasive Candidiasis during last three decades have been reported in several studies, among all Candida species the Candida albicans is considered as the most common infectious agent the other non-albicans like C. Tropicalis, C. glabrata, C. parapsilosis C. krusei, and C. dubliniensis were raised as infectious agents. The aim of current study is to characterize the candida species from the clinical specimens of patients admitted in the ICU of Tertiary Care hospital in Eastren Nepal and to perform their antifungal susceptibility.

Material and Methods

The study was carried out in the tertiary care hospital Nobel Medical College and Teaching Hospital Biratnagar Nepal over a period of 6 months between September 2015 to February 2016. The following techniques were employed to characterize the isolates in the study – Gram's stain, culture on Sabouraud's Dextrose Agar, Germ Tube test, morphology in Cornmeal Agar and chromogenic agar media, sugar fermentation and sugar assimilation tests, and the results were interpreted by using standard protocols.

Results

Out of 50 candida isolates from different clinical samples including 37 blood samples, 9 urines and 4 Endo Tracheal (ET) tube, the most common species was C.albicans (44%) followed by C.tropicalis (26%), C.Glabrata (18%), C.Parapsilosis (08%), C.Krusei (02%), and C.Dubliniensis(02%).

Conclusion

The purpose of the study is to show the value of species isolation, identification and antimicrobial sensitivity testing of the ICU & NICUs patients.

Key Words: *Antifungal susceptibility, Candida species, Candida bloodstream infections (BSIs), Intensive Care Unit, Non- Candida albicans species.*

Introduction

For over 20 years, Candida bloodstream infections (BSIs) have been increasing

significantly worldwide, representing an important infective complication in hospitalized patients with medical and

surgical disorders [1]. *Candida* spp. especially *Candida albicans* consider as one of the most common cause of fungal infections leading to a range of life-threatening invasive too non-life-threatening mucocutaneous diseases [2]. According to nosocomial Infection Surveillance systems of the United State, *Candida* spp. is the 7th most common nosocomial pathogens [3]. There are several *Candida* species involve in causing disease, but the most commonspecies is *Candida albicans*. Many other documents and records are showing the increasing incidence of other non-*albicans* among hospitalised and immune suppressed patients. The emergence of this opportunistic pathogen is favoured by the change in the most susceptibility due to the growing number of immune compromised individuals in the population as a result of HIV pandemic and the use of long-term immunosuppressive therapy in cancer and organ transplant patients [4]. *Candida* infection in hospitalized patient is increasing significantly over the last 10 years. Particularly the patients in the Intensive Care Unit who have invasive monitoring lines. *Candida* infection leading to prolonged hospitalization and significant mortality which dictate the need to take all the possible measures to prevent this infection particularly at the high risk patients.

Among the ICU patients *Candida* bloodstream infection has become the fourth common organism because of the invasive infection in critical patients) [5,6]. In recent year there has been increase in isolation of other species from neonate's patients but still the *Candida albicans* is the most common one with invasive Candidiasis [7]. The causative agents of bloodstream infection is most commonly by *Candida albicans* with prevalence rate is near by 50%) [8]. The increasing nosocomial UTI subgroups is because of

fungal infection and all fungal UTI are due to *Candida* species) [9].

Materials and Methods

The study was undertaken with the *Candida* isolates obtained from clinical specimens of patients admitted in the ICU for a period of 6 months from September 2015 to February 2016, in the Department of Microbiology in a tertiary care hospital Nobel Medical College and Teaching Hospital Biratnagar Nepal, It has a 30 bedded ICU. The study was recruited after approval of Institutional Review Committee (IRC).

Selection of cases & inclusion criteria:

1. patients with different indwelling devices admitted in ICU.
2. patients with long term corticosteroids therapy like immune compressive and HIV.
3. premature low birth baby admitted in ICU
4. patient with major surgery admitted in ICU.

Exclusion Criteria

- 1.Those clinical samples which shows growth other than *Candida* from ICU patients.

2. Patients with antifungal therapy.

Microbiological records of ICU from during the period of 6 months were reviewed to identify the Patients with positive *Candida* cultures. Sample collected were used to inoculate on Sabourad Dextrose Agar with chloramphenicol slant and for direct microscopy with Gram's stain. Culture growths were subjected to Germ tube test and corn meal agar(CMA) morphology (Dalmau technique) & CHROM agar [10]. Carbohydrate assimilation & fermentation test to differentiate between *Candida albicans* and non-*albicans* groups. The susceptibility to antifungal drugs of *Candida* isolates was determined by using the Disk Diffusion method described by the Clinical and Laboratory Standards Institute (CLSI, USA), document M44-A [11]. The

specimen collected was blood, ET tube and urine. Positive Candida culture patient's data, clinical features, risk factors, and results were taken for further management.

Results

A total of 186 samples were received, from the ICU of our hospital during the study period. Out of these 50 samples showing growth of candida were included. In this study, among the 50 Candida species isolated, C. Albicans were more in number than NCA species. Out of 50 candida isolates from different clinical samples including 37 blood samples, 9 urines and 4 Endo Tracheal (ET) tube [table no1], the most common species was C. albicans (44%) followed by NCA species C. tropicalis (26%), C. Glabrata (18%) %, C. Parapsilosis (08%), C. Krusei (02%), and C. Dubliniensis (02%) [table no 2].

The highest number of samples were received in the age group of 0-2 Month (42%), followed by the age groups of 3-11 Month (04%), 1-5 year (04%), between 6-12 year (04%), between 13-19 year(02%), Between 20-30 year(08%) Between 31-40 year(10%) Between 42-50year(10%) Between 51-60 year (08%), Between 61-70 year (08%) [table no 3].

Candida species were isolated more in males (54%) than females (46%) in the present study. [Table 4] Candida species were isolated mainly from blood samples (74%), followed by urine(18%) and ET tube (8%). The distribution of candida spp. From various clinical samples is in [Table No. 6]

Table 1: Distribution of samples showing growth of candida species

Samples	NO- %
Blood	37 (74%)
Urine	9 (18%)
E .T tube	4 (8%)
Total	50

Table 2: Species of candida isolated

Candida spp.	NO of isolates (%)
C.albicans	22 (44%)
C.tropicalis	13 (26%)
C.parapsilosis	04 (08 %)
C.glabrata	09 (18%)
C. krusei	01 (02 %)
C. dubliniensis	01 (02 %)
Total	50

The most common species of candida isolated was C.albicans forming 44 % of the total isolates . The non-albicans candida species form the remaining 56 % of the total isolates.

Table 3: Age, sex-wise and species-wise distribution of C.species

Age (month & year)	No (%)
Between 0-2 Month	21(42%)
Between 3-11 Month	02 (0 4%)
Between 1-5 year	02 (04%)
Between 6-12 year	02 (04%)
Between 13-19 year	01 (02 %)
Between 20-30 year	04 (08 %)
Between 31-40 year	05 (10%)
Between 42-50year	05 (10%)
Between 51-60 year	04 (08%)
Between 61-70 year	04 (08%)
Total	50

Table 4: Sex wise

Males No (%)	Females No (%)
27 (54%)	23(46%)

Table No 5: Distribution of Candida spp. From various clinical samples

Candida spp.	Blood	Urine	E. T.Tube	Total (%)
C. albicans	19(51.3 %)	02(22.2 %)	01(25 %)	22(44 %)
C.tropicalis	09 (24.3%)	03(33.3 %)	01(25 %)	13(26 %)
C.glabrata	07(18.9 %)	01(11.1 %)	01(25 %)	09(18 %)
C.parapsilos is	01(02.7 %)	02(22.2 %)	01(25 %)	04(08 %)
C. dubliniensis	01(02.7 %)	-	-	01(02 %)
C. krusei	-	01(11.1 %)	-	01(02 %)
Total	37	09	04	50

Discussion

Candida species are the most common cause of fungal infections, leading to a range of life-threatening invasive to non-life-threatening mucocutaneous diseases. The species are endogenous in nature and are usually responsible for opportunistic infections. In addition, using several broad spectrum antibiotics, immunosuppressive and corticosteroids drugs in ICUs and NICUs wards, were increased candiduria. During the several last decades, an increasing in several opportunistic fungal infection was observed.

This is newly recognized opportunistic pathogen that has been linked to oropharyngeal Candidiasis in HIV-infected patients. It has also been observed in blood isolates from bone marrow transplant patients, denture wearers, cancer patients, infants and elderly, oral and vaginal isolates from non-HIV-infected patients [5,6,7]. In this study total 186 patient's samples were screened, out of these 50 were positive for Candida. Candida was mainly isolated from blood (74%) and urine (18%) & ET Tube 8%. Candida albicans, Candida tropicalis, Candida glabrata causes 44%, 26% and 18% of the infections respectively. Our study shows Candida albicans is the most predominant one. Candida species are the 4th most causative agents of bloodstream infection in hospitalised patients due to the normal microbes of human, which enhance to colonise the implanted devices of the host [12]. Although there is low sensitivity of conventional culture to detect yeast but the invasive nature of the fungi causing opportunistic infecting which causes morbidity and mortality in hospitalized patients. The main aim of our study is to show the morbidity of fungal infection in ICU patients [13]. The advance technique of modern medicine is able to treat many kinds of disease. The incidence of nosocomial infection of the fungi have been increasing due to immunosuppressive

drugs, use of broad-spectrum antibiotics, indwelling devices, prolonged stay in the ICU, intra-abdominal surgery, immunocompromised and immunosuppressive drugs [14]. Various reports regarding the prevalence of Candida albicans and non-Candida albicans bloodstream infection have been reported from India. From the neonates Candida albicans as the most common isolates Candida few case have documented [15,16]. Candida bloodstream infection has become challenge in critically ill patient due to immuno-compromised, diabetes, intravenous cannulae, and intravenous drug use) [17]. Candidiasis is most commonly seen in ICUs patients. C. albicans is the predominant cause of Candida bloodstream infection [18]. The major component of cell membrane is phospholipids which is catalysed by phospholipase which acts as a virulent factor and due to this there was hydrolysis of phospholipids and lyses of cell [19]. Invasive fungal infections caused by a variety of fungal species are becoming an increasing problem worldwide. In particular, Candida species have become the seventh most common cause of nosocomial sepsis in children [20]. ICU patients are at higher risk for Invasive Candidiasis than patients the general ward patients [21]. Among the known risk factors for Invasive Candidiasis, colonization is the most important one as it indicates that patients have an endogenous source of candida [22]. The present study highlights the change in epidemiology in the species distribution of Candida and also highlights a rise in the infections by NCA species as compared to those by C. albicans, along with an increase in resistance of these NCA species to the routinely used antifungals. Therefore, knowledge of the local species distribution of Candida through presumptive identification, followed by confirmation, is essential to initiate early empirical therapy,

especially in an ICU setup, which harbors a lot of immunocompromised patients and other patients susceptible for acquiring various fungal infections. Moreover, antifungal susceptibility testing, though not as routinely performed as antibacterial susceptibility testing, should be carried out, along with MIC values of the isolates for the various groups of antifungals, in order to optimize therapy and outcome.

Conclusion

This study demonstrates the importance of species identification and antifungals susceptibility testing for hospitalized patients in ICUs and NICUs wards. In the NICU, it is associated with a very high mortality, especially with antibiotic uses. Major risk factors are prolonged ventilation (>7 days). Antenatal care has a protective impact on neonatal fungal infection in our settings.

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Case Report

Unilateral Basal Ganglia Hyperdensity in a Previously Undiagnosed Diabetic Patient Presenting with Hemichorea-Hemiballism (Hchb)

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Abstract

Non-ketotic hyperglycemia induced hemichorea-hemiballism (HCHB) is a rare condition with characteristic neuroimaging findings in a diabetic patient. This paper reports a 61-year-old male previously undiagnosed diabetic patient presenting with HCHB as the first presentation of diabetes.

Key Words: *Basal ganglia hyperdensity, Computed tomography (CT) scan, Diabetes mellitus, Hemichorea-hemiballism, Non-ketotic hyperglycemia.*

Introduction

Hemichorea-hemiballism associated with hyperglycemia is a rare and potentially reversible condition in a patient with non-ketotic hyperglycemia [1] and was first described by Bedwell in 1960 [2]. Literature describes this condition occurring most frequently in elderly patients with type II diabetes mellitus and majority are female and Asians [3, 4].

Neuroimaging studies of these patients show characteristic findings of contralateral basal ganglia hyperdensity in non-contrast Computed tomography (CT) scan, corresponding with T1 shortening in contralateral basal ganglia in Magnetic resonance imaging (MRI) [3-5].

However, HCHB as a rare presenting manifestation of type II diabetes mellitus in patients with no previous history of diabetes has been described and should always be thought of in elderly patients presenting with HCHB [5-9].

Case Presentation

A 61-year-old male presented to emergency department of our hospital with

two days history of involuntary movements of right upper and lower limbs. There was no past history of hypertension, diabetes mellitus, trauma, stroke, movement disorders or intake of neuroleptic drugs, with no family history of similar illness or other movement disorders. On examination he was fully conscious and oriented. HCHB of right upper and lower limb was present. Muscle strength and tone were normal. Blood glucose level was 494 mg/dl and HbA1c was 7.8 %. On urinalysis no ketones were detected. Diagnosis of type II diabetes mellitus with non-ketotic hyperglycemia was made and patient was referred for CT scan of brain. Non-contrast CT scan of brain showed hyperdensity of left lentiform and caudate nucleus with sparing of anterior limb of left internal capsule. No surrounding edema or mass effect was seen. There was no change in appearance of lesion on post contrast images. No other significant intracranial abnormality was seen. (Figure 1).

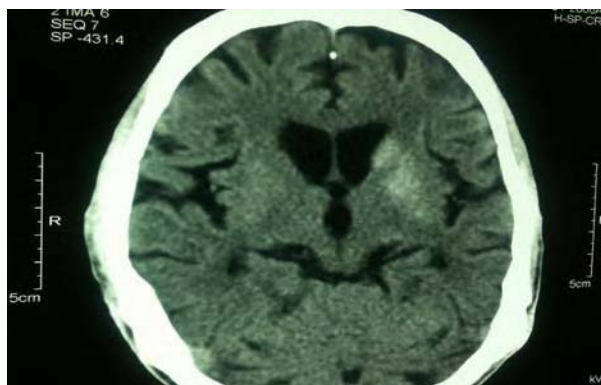


Figure 1: Non-contrast CT scan of brain showing hyperdensity of left lentiform and caudate nucleus.

Patient was treated with insulin and oral hypoglycemic agents for elevated blood sugar level. Haloperidol was given for involuntary movements. With treatment blood sugar level was restored too normal and marked symptomatic improvement was seen. After a week of treatment HCHB completely disappeared.

Discussion

Even though HCHB associated with non-ketotic hyperglycemia is mostly seen in previously diagnosed diabetic patients with poor glycemic control, there are literatures describing HCHB as a rare presenting manifestation of diabetes [5-9], as in this case. In these patients, the characteristic neuroradiological findings are seen in basal ganglia contralateral to the side of the patient's symptoms as seen in present case, with putamen involved in all cases and no isolated involvement of caudate nucleus or globus pallidus [3]. CT scan of brain shows non-enhancing hyperdensity in contralateral basal ganglia. Similarly, MRI scan of brain shows hyperintensity in contralateral basal ganglia in T1 weighted images, whereas T2 weighted / FLAIR images show hypo or isointensity. Although findings are characteristically seen unilaterally, changes in bilateral basal ganglia may be noted [3-5, 10, 11].

The exact underlying pathophysiology for radiological changes seen in non-ketotic

hyperglycemia induced HCHB are not clearly known. There are various theories for this, which includes blood hyperviscosity, depletion of gamma aminobutyric acid (GABA) and acetylcholine, ischemia, petechial haemorrhage, calcium deposition, metabolic acidosis, myelinosis, gliosis with abundant gemistocytes and manganese accumulation on gemistocytes [6, 12, 13]. Various differential diagnosis depending upon clinical and imaging findings of chorea, basal ganglia hyperdensity and T1 basal ganglia hyperintensity are described, that includes intracranial hemorrhages, cerebral ischemia, vasculitis, drugs, central nervous system lupus, multiple sclerosis, basal ganglia calcifications, chronic hepatic encephalopathy, manganese toxicity (following long term parenteral nutrition), hypoglycemic coma, neurofibromatosis, Wilson disease, Fahr disease and carbon monoxide poisoning, which can be excluded depending upon other clinical and imaging findings in these conditions [5, 13, 14].

The clinical improvement and resolution of symptoms in these patients with HCHB occurs once blood glucose level returns to normal. Also the radiological abnormalities in basal ganglia will resolve over a period of time [13].

Conclusion

Non-ketotic hyperglycemia induced HCHB may be the first presenting manifestation of type II diabetes mellitus and should be considered in differential diagnosis of patients, especially elderly presenting with involuntary movements. It has characteristic neuroimaging findings, and together with clinical findings early recognition of this condition is important as it is easily treatable and correction of hyperglycemia leads to spontaneous resolution of symptoms.

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