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Child Sexual Abuse – The Current Scenario

Ayesha Taniya P H*, Niranjana Rajesh*, Anu Sasidharan*

ABSTRACT
Child Sexual Abuse (CSA) is prevalent all over the world. The dynamics of CSA is very different from Adult Sexual Abuse and therefore cannot be considered in the same way. It is said that 90% of the perpetrators of CSA are known to the child. The ravages of CSA are deep seated and lifelong. Victims of CSA are much more prone to major depression, anxiety disorder, suicidal ideation, suicide attempt, alcohol dependence, illicit drug dependence, post traumatic stress disorder (PTSD) symptoms, decreased self-esteem, and decreased life satisfaction. The prevalence of CSA in India is 52.94% of boys and 47.06% of girls. In 2012, ‘The Protection of Children from Sexual Offences Act (POCSO Act) 2012’ was passed. This protects children and criminalizes sexual assault, harassment and pornography involving a child. In spite of POCSO, there is still a lot to be done to protect children from CSA.

Keywords: Child Sexual Abuse (CSA), Perpetrators, POCSO Act, PTSD, Psychological effects, UNICEF, WHO

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INTRODUCTION
Child Sexual Abuse (CSA) is prevalent all over the world, and has many long term deleterious effects on a child. The World Health Organisation (WHO) has defined CSA as “the involvement of a child in sexual activity that he or she does not fully comprehend, is unable to give informed consent to, or for which the child is not developmentally prepared and cannot give consent, or that violates the laws or social taboos of society”. Child sexual abuse is evidenced by this activity between a child and an adult or another child who by age or development is in a relationship of responsibility, trust or power, the activity being intended to gratify or satisfy the needs of the other person. This may include but is not limited to the exploitative use of a child to be engaged: in any unlawful sexual activities; in prostitution or other unlawful sexual practices and in pornographic performance and materials1.

While sexual abuse in adults and children seem comparable in theory, the dynamics of the two are very different. In CSA, the perpetrators use manipulation, threats and promises of love to gain the child’s trust and hide the abuse. CSA often occurs over weeks, months and sometimes years. The perpetrators “groom” the child, and the intensity of the abuse gradually increases over a period of time. This as opposed to sexual abuse in adults, is usually an isolated event, with involvement of force1.

Prevalence of CSA In The World
The WHO concluded in 2002 that 150 million girls and 73 million boys have experienced sexual violence before the age of 18.2 In 2016, The WHO claimed that 1 in 5 women and 1 in 13 men report having been sexually abused as a child. The National Criminal Justice Reference Service reported that 1 in 15 US adults reported to have had forced intercourse at least once in their life-time. According to a 2009 meta-analysis which studied prevalence over 22 countries - 7.9% of men and 19.7% of women globally experienced sexual abuse prior to the age of 18.4

- The highest prevalence rate of child sexual abuse was found in Africa (34.4%),4 followed by America and Asia which had prevalence rates between 10.1% and 23.9%. Europe showed the lowest prevalence rate with 9.2%2.
- South Africa has the highest prevalence rates for both men (60.9%) and women (43.7%)4.
- For women, seven countries reported prevalence rates above 20%; Australia (37.8%), Costa Rica (32.2%), Tanzania (31.0%), Israel (30.7%), Sweden (28.1%), United States (25.3%) and Switzerland (24.2%)4.
- Whereas for men, Jordan presented with the second highest prevalence for sexual abuse with 27%4.

Another study which assessed the prevalence in 24 countries found that prevalence of CSA varied from 0-69% in girls and 0-47% for boys. In this, 9% of girls and 3% of boys have undergone forced intercourse. Moreover, 15% of girls and 7% of boys have suffered mixed sexual abuse5.

The Centres for Disease Control and the US Department of Justice conducted a study in the US and reported prevalence of being forced to have sex at some point of time in their lives as 11% and 4% of the high-school girls and boys, respectively4. A review of studies from 21 high- and middle-income nations showed that 7-36% of females and 3-29% of males reported being victims of sexual abuse during their childhood6. Few investigators conducted a study in Brazil in 2009. It was found that 5.6% of girls and 1.6% of boys were sexually abused. 60% of these incidents took place when the victims were younger than 12 years old. It was also found that boys were to be abused at younger ages in comparison to girls. CSA is accountable for about 1% of the global

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burden of disease, but it is likely to be a risk factor for several other conditions like alcohol consumption, illegal drug usage, development of mental disorders, and spread of sexually transmitted diseases, which when pooled, are accountable for over 20% of the global burden.

Similarly in China a study concluded that 33% of the participants were victims of CSA.8 Another study done in Boston concluded that the burden of CSA was 26.7% and 16.7% in girls and boys, respectively.9 In Mexico, one research work reported a prevalence of 18.7% of CSA (58% in girls and 42% in boys). Physical abuse was involved in 75% of the cases10. In Croatia, 10.8% of the children reported as having faced some form of CSA during childhood11.

Prevalence of CSA in India

Nineteen percent of the world's children live in India. According to the 2001 Census, some 440 million people in the country today are aged below eighteen years and constitute 42 percent of India's total population i.e., four out of every ten persons. With growing concerns about the child rapes and institutional abuse, the Ministry of Women and Child Development conducted a study in India about the prevalence of child abuse in the country. The study, based on a well-designed methodology, covered 13 states (two states from each of the six geographic zones in the country) including states with the highest through to the lowest crime rates incidence of offences against children.6

Out of 12,447 child respondents, 52.94% of boys and 47.06% of girls were found to be sexually abused. From these, 21% reported being subjected to severe forms of sexual abuse. This means that across the country - every second child was being subjected to other forms of sexual abuse and every fifth child was facing severe forms of sexual abuse. For these reported cases of CSA, majority of the perpetrators were6:

- Uncles or Neighbours (31%)
- Friends/ Classmates (29%)
- Cousins (10%)
- Employers (9%)

Remaining 21% children reported sexual assault by others that included strangers, persons they were faintly acquainted with, teachers, care givers, etc. When one looked within the evidence groups, the highest percentages of children reporting sexual assault were6:

- Working children (8.70%)
- Children in institutional care (7.08%)
- Street children (6.53%)

Assam, Andhra Pradesh, Bihar and Delhi reported the highest incidence of sexual abuse of both boys and girls and Goa reported the lowest prevalence amongst boys and girls. Majority of children subjected to sexual assault kept quiet (72.1%) and did not report the matter to anyone. Among those who reported, the majority of children shared the incident with their parents followed by brother and sister (6.7%). Only 3.4% children reported the matter to police6.

The prevalence of CSA in Kerala was found to be 55.04% in boys and 44.96% in girls. Out of these 21.22% of boys and 13.84% of girls experienced severe forms of sexual abuse. This shows that the prevalence of CSA in Kerala is at par with the national statistics. This seems surprising as Kerala has the highest literacy rate in the country, and so one would assume that the prevalence of CSA might be lower6.

Perpetrators and Other Associated Factors of CSA

It is said that 9 out of 10 perpetrators of CSA are known to the child, with only 10% of strangers accounting as perpetrators of CSA. Approximately 30% of victims of CSA are sexually abused by family members. The younger the victim, the more likely it is that the abuser is a family member. Of those molested under the age of6, 50% of perpetrators were family members. About 60% of the victims are abused by people their family trusts12.

It is also seen that the younger the child is, the more likely it is that the offender is a juvenile. Forty three percentage of perpetrators of CSA (where victims were below 6 years) happen to be juveniles13.

Most incidents of CSA occur in residences, typically that of the victim or perpetrator – 84% for children under age 12, and 71% for children aged 12 to 1713.

Though all children are at risk of sexual abuse, children living with step parents, single parents, single parents with a boyfriend/girlfriend and foster children seem to have a higher risk of being sexually abused. Children in low socioeconomic status households, rural area also are seen to have a higher risk14.

The low incidence of CSA seen in boys may be due to not reporting it from fear of “looking weak” (if the offender was a female) or being viewed as homosexual (if offender was a male)13. Age is also a factor, where children seem to most vulnerable at ages 7–13. It is also found that children who are victims of other crimes have a higher risk of being sexually abused15.

Sequealae of CSA

The ravages of abuse are deep seated and often lifelong. The evidence suggests that sexual abuse is an important problem with serious long-term effects. Abuse is unique in the way it damages children because it leaves the survivor with shame, intimacy issues, or even low self esteem as a result of their experience that could haunt them for well into their adulthood. Child Sexual Abuse is associated with substantial increased risk of subsequent psychopathology.

Although a wide variety of psychological sequelaes have been documented in sexually abused children referred for evaluation or treatment, there appears to be considerable variability in the severity of the symptoms,
and we remain ignorant of these sequelae in the abused children who never enter the mental health system. A study in the United States shows that those who experience Child Sexual Abuse are more likely to be diagnosed with mental disorders, have suicide-related problems and are at increased likelihood for experiencing adult victimization.

Meanwhile, a study done in New Zealand concludes that the extent of exposure to Child Sexual Abuse was associated with increased rates of: major depression, anxiety disorder, suicidal ideation, suicide attempt, alcohol dependence, and illicit drug dependence. In addition, at age of 30 years Child Sexual Abuse was associated with higher rates of post traumatic stress disorder (PTSD) symptoms, decreased self-esteem, and decreased life satisfaction. Childhood sexual abuse was also associated with decreased age of onset of sexual activity, increased number of sexual partners, increased medical contacts for physical health problems and welfare dependence.

An article showing a study aimed at comparing the socio-demographic, abuse-related, and clinical features of female adolescents who were sexually abused by different perpetrators, and identifying the factors associated with suicidal and non-suicidal self-injury (NSSI) concluded that Major Depressive Disorder was the most common psychiatric diagnosis, which was present in 44.9% of the cases. Among all the victims, 25.6% had attempted suicide, 52% had suicidal ideation, and 23.6% had NSSI during the post-abuse period.

In a prospective investigation the results supported the notion that childhood sexual abuse may be a risk factor for early and risky sexual activity and teenage motherhood. Sexually abused participants have reported: being significantly younger at the age of voluntary intercourse, less birth control efficacy, were younger at the birth of their first child, and were more likely to be teen mothers than were comparison participants.

Abuse in childhood could interfere with the development of the child; affect regulation and interpersonal relatedness, which would impact on the individual's awareness of danger and ability to respond to threatening situations, hence leading to an increased risk of re-victimization. Secrecy and stigmas associated with Child Sexual Abuse may lead to reluctance to seek mental health treatment, and increased risk of experiencing mental health impairment including suicide attempts.

**Detecting Sexual Abuse in Children**

Since there are no behavioural signs or symptoms that clearly indicate the presence of sexual abuse, physicians must examine and observe children with a high degree of suspicion.

The child's disclosure is the most important part of detecting sexual abuse. Children must be interviewed, preferably alone, using open ended questions like “Has anyone ever touched you in a way that made you uncomfortable or in a way that you didn't like?” It is important to keep a neutral tone, and to not ask leading questions.

There are certain behaviours that are more suggestive of sexual abuse like sexualized behaviour. This can vary depending on the developmental stage of the child. In very young children it can be compulsive masturbation, preoccupation with the sexual parts of others or performing developmentally inappropriate sexual acts. In older children it can mean promiscuous behaviour or unusually sexualized way of dressing or acting.

Another common set of behaviours are “post traumatic” symptoms. These include high levels of anxiety, fearfulness of certain places or people.

Other behaviours are depression, aggressiveness, eating disorders, self harm/ self abuse, school problems of sudden onset, suicidal tendencies, and substance abuse.

**Physical Findings in Victims of Child Sexual Abuse**

It is now well acknowledged that, unlike physical abuse, very few cases sexual abuse can be diagnosed on physical examination alone. Summaries from nearly two dozen studies show that 50% of sexually abused girls and 53% of sexually abused boys appear entirely normal on physical examination. Nonetheless, it is recommended that all children of suspected sexual abuse must be fully examined.

Most patients have normal and nonspecific findings on examination. These findings include the following:

1. Hymenal tags, bumps or mounds
2. Labial adhesions
3. Clefts or notches in the anterior half (between the 9- and 3-o'clock position) of the hymen
4. Vaginal discharge
5. Erythema of the genitalia or anus
6. Perianal skin tags
7. Anal fissures
8. Anal dilatation with stool in the ampulla.

Physical findings that are concerning but not diagnostic of sexual abuse include the following:

1. Notches or clefts in the posterior half of the hymen extending nearly to the vaginal floor
2. Condylomata acuminata in a child older than two years who gives no history of sexual contact
3. Immediate, marked anal dilatation

Physical findings that are diagnostic of penetrating trauma include:

1. Acute laceration or ecchymosis of the hymen
2. Absence of hymenal tissue in the posterior half
There should be regular classes by a trained professional on good touch and bad touch. Children seen in the emergency rooms should be given a brief examination to screen for sexual abuse. In one study, the records of 26,000 children seen in the emergency department of a teaching hospital over an 18-month period were analyzed. Three hundred of those patients were identified by medical staff as victims of sexual abuse [21].

Increased concern and awareness of the despair of children and prevalence of CSA in the country by the public and social media may account for the Government of India passing a special law called, ‘The Protection of Children from Sexual Offences Act (POCSO Act)’ [22]. This Act criminalises sexual assault, sexual harassment, and pornography involving a child (less than 18 years of age) and mandates the setting up of Special Courts to expedite trials of these offences. This is the first time that an Act has listed aspects of touch as well as non-touch behaviour (eg: photographing a child in an obscene manner) under the ambit of sexual offences. For more heinous offences of Penetrative Sexual Assault, Aggravated Penetrative Sexual Assault, Sexual Assault and Aggravated Sexual Assault, the burden of proof is shifted on to the accused.

The Act further incorporates child friendly procedures for reporting of offences, recording of evidence, investigation and trial of offences. Even the attempt to commit an offence and abetment of the offence has also been made liable for punishment under the Act [22].

**RECOMMENDATIONS AND CONCLUSION**

Sex has always been a taboo topic in India. This is usually where the problem begins. Most children don’t know that they’re being abused because sexual abuse has not been spoken about at home, and the few children who do know about it don’t feel free enough to tell anyone. Most of the time, when children do tell an adult about their abuse, they’re made to keep quiet about it because of the social stigma and the shame that is associated with sexual abuse, which ends up affecting the victim. This has to stop if we ever want to overcome this problem. Awareness and knowledge have always been key to bringing about change. As Child Sexual Abuse has major impact on the psychological, physical and reproductive health of individuals, it is the responsibility of the medical community to take a more active role in detecting, treating and preventing child sexual abuse.

- Parents must be counselled and taught the signs to look out for and to detect probable sexual abuse in children by medical professionals from the very beginning.
- There should be regular workshops for teachers on how to detect and deal with a sexually abused child by professionals specialized in the field.
- There should be regular classes by a trained professional on good touch and bad touch and body ownership in schools.
- Physicians must be alert, and must interview the child, preferably alone, about sexual abuse.
- It has also been suggested that all children seen in emergency rooms should be given a brief examination to screen for sexual abuse. In one study, the records of 26,000 children seen in the emergency department of a teaching hospital over an 18-month period were analyzed. Three hundred of those patients were identified by medical staff as victims of sexual abuse [21].
- All schools must have a trained counsellor, who is well equipped to detect and deal with victims of sexual abuse.
- During the school health programme, physicians must carefully bring up the subject and ask the child for history of sexual abuse.
- More research must be done about child sexual abuse.

**REFERENCES**

8. Song Yi, Ji C, Agardh A. Sexual coercion and health-risk behaviors among urban Chinese high school students. Glob Health...
High Burden of Cardiovascular Diseases in Kerala: High Time to Reorient the Primary Health Care System

Rakesh P S*

ABSTRACT
Kerala, a state in southern India, with a population of 33.4 million, has made impressive improvements in its people’s conditions of living. Despite having a low per capita income, Kerala’s indicators of health and social development—such as the human development index (0.84), life expectancy at birth (75 years), infant mortality rate (06/1000 live births), sex ratio (1084 females to 1000 males), and female literacy rates (92.07)—are comparable to those of many developed countries. These faster demographic transitions in the state have been attributed to be the results of a political environment that emphasized rights, a policy thrust that ensured rights in education and health and a reasonably strong primary health care system with good infrastructure of primary health centers.

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Burden of Cardiovascular Diseases in Kerala
However, Kerala which seems to have entered into the fourth stage of the epidemiological transition is now facing a huge threat due to alarmingly rising trends of Non communicable diseases (NCD). Cardiovascular diseases (CVDs) have become the leading cause of mortality in Kerala contributing to as much as 40% of all deaths while the proportion of deaths due to infectious diseases was 5% and due to maternal and perinatal conditions was less than 1%. There are no representative surveillance data on the prevalence of CVD and the secular trends of CVD mortality in the state. However, a well conducted cohort study has shown that the age adjusted death rate due to cardiovascular diseases in the state is 490 and 234 per 100,000 for men and women respectively every year, which is far higher than the figures for many industrialised countries. A multi-centric study in the state has shown that the age-adjusted prevalence of definite IHD is 3.5%, thrice as high as the figures two decades ago.

Determinants of CVD in Kerala
Multi-centric studies done in India by different agencies have shown that the prevalence of CVD risk factors are markedly high in Kerala as compared to the other states in the country. Kerala has high prevalence of most known risk factors of CVD like tobacco smoking: men- 39.7%, women-0.4%, overweight (BMI> 25.0 kg/m²): men- 23.9%, women- 37.5%, unhealthy diet (< five servings of fruits and vegetables/day): men-42.9%, women-50.9%, diabetes (fasting blood sugar > 126 mg/dl or on 3 medication): men-14.3%, women-17.8%, hypercholesterolaemia (total cholesterol >200 mg/dl): men-51.4%, women-61.5% and hypertension (JNC VII): men-33.9%, women- 31.6%.

There was not much urban-rural differences in the prevalence of IHD in the state. A rise in the prevalence of CVD in the state has been attributed to changes in lifestyle and dietary practices in the state which in turn has been attributed to the rapid urbanisation that happened in last two decades. A multi-centric study in the state has shown that the age-adjusted prevalence of definite IHD is 3.5%, thrice as high as the figures two decades ago.

Current policies and programs for CVD prevention
Recognising the problem, State Government has initiated own program in 2007 for combating NCDs- first of its kind in the country. The program aimed at early diagnosis and treatment of NCDs particularly Diabetes and Hypertension where multi- purpose health workers do screening at community and refer them for treatment and follow up care to the medical doctors at primary health centre. Medicines were provided free of cost at the Primary Health Centre. However, a recent evaluation of the NCD control program in the state highlighted that the program did not focus much on primodial and primary prevention interventions. NCD control program has now been also operating through National Program for the Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke by Government of India which focuses on screening for risk factors, health promotion, and health education advocacy at various settings. Government of Kerala is committed to attain Sustainable Development Goals and has formulated strategies for the same. Key targets for NCD control include a 30% reduction in premature mortality.
<table>
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<tr>
<th>Authors</th>
<th>Year</th>
<th>Study sample</th>
<th>Description of study</th>
<th>Major Findings of the study</th>
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<tr>
<td>Kutty VR et al&lt;sup&gt;6&lt;/sup&gt;</td>
<td>1993</td>
<td>1253 adults in Trivandrum</td>
<td>Cross sectional</td>
<td>Prevalence of Definitive Coronary Artery Disease was 1.4%, Obesity 5.5%, Diabetes 4%, Smoking 21.5%, Hypertension 17.9%</td>
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<tr>
<td>PROLIFE&lt;sup&gt;3&lt;/sup&gt;</td>
<td>2002-2007</td>
<td>161942 people from 7 villages in Trivandrum</td>
<td>Cohort study, 4272 deaths recorded in 5 years</td>
<td>Prevalence of Definitive Coronary Artery Disease was 1.4%, Obesity 5.5%, Diabetes 4%, Smoking 21.5%, Hypertension 17.9% Age-standardized cardiovascular disease (CVD) death rates were 490 for men and 231 for women per 100 000 person years</td>
</tr>
<tr>
<td>Satish et al&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2003 And 2010</td>
<td>2510 15-64 years Trivandrum</td>
<td>Followed up same individuals after 7 years.</td>
<td>Over a seven year period, several NCD risk factors have increased in the study cohort. There were significant increases in weight (mean change +5.0 kg, 95% CI 4.2 to 5.8), Physical inactivity (OR 2.0, 95% CI 1.3 to 3.0), obesity (OR 2.2, 95% CI 1.7 to 2.8), and central obesity (OR 1.9, 95% CI 1.5 to 2.3) increased.</td>
</tr>
<tr>
<td>Thankappan et al&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2007</td>
<td>7449 individuals between 15-64 years</td>
<td>Part of ICMR Multicentre survey</td>
<td>Tobacco (21.9%), Alcohol (11.1%), low fruit and vegetable intake (39.7%), physical inactivity (6.8%), overweight (24.9%), hypertension (28.8%), Diabetes Mellitus (14.8%), Hypercholesterolemia (54.1%)</td>
</tr>
<tr>
<td>IDSP Risk factor survey&lt;sup&gt;7&lt;/sup&gt;</td>
<td>2007-2008</td>
<td>5000 households from the state</td>
<td>Survey Conducted in 7 states</td>
<td>Obesity (43%) prevalence highest in Kerala as compared to other states. Fruits consumption less than 5 servings-87%, Low physical activity-76% and Hypertension-24%</td>
</tr>
<tr>
<td>Sreedharan et al&lt;sup&gt;9&lt;/sup&gt;</td>
<td>2009</td>
<td>741 000 urban and 185 000 rural people Trivandrum</td>
<td>Prospective Study- 541 stroke events in 6 months</td>
<td>Adjusted annual incidence rates for Cerebrovascular disease per 100 000 was 135 (95% CI123 to 146) for total, 135 (122–148) for urban, and 138 (112–164) for rural populations.</td>
</tr>
<tr>
<td>Mohanan et al&lt;sup&gt;4&lt;/sup&gt;</td>
<td>2012</td>
<td>25278 Acute Coronary Syndrome admissions from 125 hospitals</td>
<td>Prospective data collection during 2007-2009 from ACS Registry</td>
<td>60% of Acute Coronary Syndrome occurred in patients less than 70 years of age; 22% below 50 years</td>
</tr>
<tr>
<td>Krishnan et al&lt;sup&gt;5&lt;/sup&gt;</td>
<td>2012</td>
<td>5167 adults, Multi stage cluster random sampling</td>
<td>Cross sectional</td>
<td>Prevalence of any IHD was 12.5 % Physical inactivity- 17.5%; overweight or obese-59 %, abdominal obesity- 57 %, Hypertension- 28 %, diabetes- 15 %, high total cholesterol -52 %. No urban-rural difference in CAD prevalence.</td>
</tr>
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</table>

Table 1: Summary of major studies done in Kerala state regarding Cardio Vascular Disease burden and its risk factors
CONCLUSION
CVD has become an important public health issue in Kerala and is one of the most important causes of mortality and morbidity in the State. There is an urgent need to reorient primary health care system in the state for better prevention and management of CVD disease and its risk factors.

Future Directions for CVD prevention
The high burden of cardiovascular morbidity in the population has to be tackled with more vigour. More resources need to be routed for applying the existing evidence base to tackle the CVD epidemic in policies, programs and capacity building. In addition to the strengthening of curative services, priority should be given to strategies for CVD prevention and health promotion. The primary health system is still behind the ‘unfinished agenda’ of the management of communicable diseases, maternal and child health care, and immunization which needs to be reoriented towards preventing cardiovascular diseases. Behaviour change communication and health promotion at schools, providing facilities for sports and physical exercise, subsidising and promoting seasonal fruits and vegetables, workplace wellness programs, standardised and quality assured care, task-shifting and task sharing interventions including involving frontline health workers and nurses for lifestyle counselling, mass education, and to ensure adherence, better use of information communication technology for CVD prevention, better surveillance and reporting systems for CVDs and risk factors, policies to address social determinants of CVD for control of primodial risk factors and having a life cycle approach for prevention are need of the hour. The capacity for CVD research needs to be built to generate contextualized evidence. Policies and programs that influence CVD need to cover a various sectors beyond the healthcare, including finance, agriculture, urban affairs, education, social justice and the environment. To be successful it requires political stewardship with community ownerships.
REFERENCES


Clinical Features and Treatment Outcomes in Axial Spondyloarthritis Patients in India: A Single Center Retrospective Analysis

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ABSTRACT

Background and aim: Axial spondyloarthritis (ASpA) is a chronic inflammatory disease routinely treated with nonsteroidal anti-inflammatory drugs (NSAIDs). Patients unresponsive to NSAIDs are treated with tumor necrosis factor (TNF-α) inhibitors. The aim of this study is to report clinical features and treatment outcomes in Indian ASpA patients.

Methods: A non-interventional, retrospective analysis of medical records of ASpA patients, obtained from a single center, between January 2014 and 30th June 2016 was performed. All patients (n=130) were initially treated with NSAIDs, and patients who had uveitis received sulfasalazine (SSZ, n=40) therapy. Treatment for patients unresponsive to NSAIDs (n=31) was modified to include anti-TNF-α biologics, etanercept (n=13) or infliximab (n=17). Changes in disease activity, in response to treatment, were assessed by recording Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) scores at 0, 6, and 12 months.

Results: Overall, BASDAI scores steadily decreased from 3.2 at baseline to 2.8 and 2.5 at 6 and 12 months, respectively, after treatment (ANOVA, p<0.0001). Similarly, overall ASDAS ESR decreased from 2.7 at baseline to 2.4 and 2.2 after treatment (ANOVA, p<0.0001).

Conclusion: Results of this study show that disease activity in axial spondyloarthritis patients reduces, from baseline to 12 months, in response to treatment.

Keywords: ASpA, disease activity, NSAIDs, anti-tumor necrosis inhibitors, biologics

INTRODUCTION

Spondyloarthritis (SpA) is a set of autoimmune inflammatory diseases which have shared clinical and genetic characteristics1. Axial spondyloarthritis (ASpA) refers to chronic inflammation involving axial skeleton components such as the sacroiliac joints and the spine. Non-radiographic ASpA without radiographic sacroiliitis and ankylosing spondylitis (AS) or radiographic ASpA are considered to be 2 stages of ASpA1. Axial spondyloarthritis is linked to HLA-B27 antigen (74%-89%) and is more prevalent in men. The diagnostic features of ASpA include lower back pain, heel pain (enthesitis), dactylitis, uveitis (30%-40%), inflammatory bowel disease (5%-10%), hip involvement (24%-36%), psoriasis (10%), asymmetrical arthritis, positive response to NSAIDs, elevated ESR or C-reactive protein level2. Structural damage occurs as a result of bone destruction and abnormal bone formation2. The molecular mechanisms involved in ASpA pathogenesis include abnormal function of antigen-presenting cells, abnormal HLA-B27, and increased production of chemokines and cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-17 (IL-17)2.

Taurog et al. provide an algorithm for diagnosing ASpA in patients who present with the most common spondyloarthritis symptom lower back pain2. The Assessment of SpondyloArthritis International Society (ASAS) established the classification criteria for ASpA based on imaging, clinical, and laboratory criteria. The diagnosis of ASpA is recognized in patients who have had 3 or more consecutive months of back pain, are <45 years of age, in whom MRI or radiography has confirmed the presence of sacroiliitis, and who have at least one clinical or laboratory characteristic of spondyloarthritis. Alternatively, patients who are HLA-B27 positive and have two spondyloarthritis clinical features are also diagnosed with ASpA2,3.

Axial spondyloarthritis disease activity is assessed using multiple tools such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS). Function is assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI), and mobility is measured with the Bath Ankylosing Spondylitis Metrology Index (BASMI)3,4.

The treatment goals of ASpA therapy include alleviating symptoms, enhancing spinal flexibility and normal posture, decreasing functional limitations, preserving the ability to work, and reducing disease complications2,3,5. Poddubnyy et al. have outlined the treatment recommendations put forth by the ASAS and European League Against Rheumatism (EULAR)5.

As per these evidence-based guidelines, the first-line therapy for ASpA includes nonsteroidal anti-inflammatory drugs (NSAIDs) and nonpharmacological treatments such as education, regular exercise, and phys-
iotherapy. NSAIDs such as nonselective or selective cyclooxygenase (COX) inhibitors reduce pain and stiffness in most ASpA patients. If NSAIDs are effective and well-tolerated, then they can be used for the long-term with dosing adjustments as per the patient’s symptoms. Common adverse effects of NSAIDs include gastrointestinal and cardiovascular events. Disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate and sulphasalazine are useful for patients with peripheral joint involvement.

In patients who are unresponsive to NSAIDs and other first-line therapy, TNF-α blockers are recommended as a second line treatment choice. All TNF-α inhibitors adalimumab, etanercept, golimumab, and infliximab are considered to be highly efficacious in reducing ASpA symptoms in nearly 40%–50% of patients who had NSAIDs therapy failure. Analgesics are recommended for patients in whom pain is not effectively controlled by other treatments. Lastly, surgery is recommended for ASpA patients with severe spinal damage that has a severe impact on the patient’s functional ability and quality of life.

Even though anti-TNF-α biologics are shown to be efficacious in ASpA patients unresponsive to NSAIDs, they are not regularly used in India because of their high cost. The cost of anti-TNF-α biologics such as etanercept and infliximab is Rs. 20,800/100 mg and Rs. 16,500/25, respectively. However, our specialist state-owned healthcare organization provides biologics for ASpA patients. Here we report a physician’s experience of biologics usage in Indian ASpA patients. The noteworthy results of this retrospective study include patient population demographics, disease activity, HLA-B27 positivity, NSAIDs efficacy, and biologics usage in NSAIDs-unresponsive Indian ASpA patients.

METHODOLOGY
Study group
This was a non-interventional, retrospective analysis of medical records of patients diagnosed with ASpA in a single center between January 2014 and June 2016. All patients (n=130) were initially treated with NSAIDs such as indomethacin (75 mg at bed time) or etoricoxib (120 mg at bedtime). Patients who had other conditions such as uveitis, psoriasis, irritable bowel syndrome (IBS), or gut disorders were also treated with 1 g sulphasalazine (SSZ, n=40, 30.8%) twice daily. After 3 months, patients who did not respond to NSAIDs (n=31) were treated with add-on anti-TNF-α biologics either 50 mg etanercept subcutaneous injection once a week (n=13, 10%) or 300 mg infliximab IV infusion once in 2 months (n=17, 13.1%).

Baseline disease activity
Four standard scales were used to assess disease activity, at baseline, before any treatment was initiated. The four scales are, Maastrich Ankylosing Spondylitis Enthesitis Score (MASES), Bath Ankylosing Spondylitis Metathology Index (BASMI), BASDAI, and ASDAS ESR scales. Changes in disease activity, in response to all treatment groups, were assessed by recording BASDAI and ASDAS ESR scores at 6 and 12 months.

Enthesitis inflammation of the tendon, ligament, or joint capsule insertions is a potential extra-axial manifestation found in spondyloarthritis (SpA) patients. Enthesitis is quantified as per the MASES scale which contains 13 pre-defined entheses. The BASMI is a 0 to 10 scale in which higher scores represent worsening disease activity. The BASDAI is a 0 to 100 scale in which higher scores indicate worsening disease activity, whereas ASDAS scale includes patient perceptions and laboratory variables such as ESR or CRP.

Statistical Analysis
Descriptive method was used to analyse the data. Counts and percentages was provided for categorical data. Continuous data was summarized using mean, standard deviation. One-way Analysis of Variance (ANOVA) was used to compare the mean BASDAI and ASDAS ESR scores for all treatment combinations. Multiple comparison was done to check which treatment groups differed from each other.

RESULTS
Demographics, Clinical presentation, and Diagnosis
Of the 130 patients, 121 (93%) were males and 9 (7%) were females. The mean age of the patient population was 31.5 years (±8.2), with a mean time to diagnosis of 53.8 months (±53.2) and duration of illness of 29.7 months (±39.7). Only 7 patients had a smoking history.

The key clinical presentation and diagnostic characteristics of the patient population are presented in Table 1. A few patients (n=5) had a family history of joint disease, while most of them (n=102, 78%) had lower back pain. In addition, majority of the patients had early morning stiffness (n=83, 64%) and nearly half (n=56) had peripheral joint involvement. Few patients had skin (n=4) and ocular (n=5) involvement. In terms of diagnosis, majority of the patients (n=93, 72%) were HLA-B27 positive. X-rays confirmed sacroiliac (SI) joint involvement in 58 (45%) patients. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated in 22 (13%) and 31 (24%) patients, respectively. Magnetic resonance imaging (MRI) test of all patients confirmed disease activity.

Disease activity assessment
The patients’ disease activity was assessed at baseline (0 months) and subsequently at 6 and 12 months after treatment. The baseline disease activity was assessed based on 4 different scales (Table 1).

Figure 1 shows that overall mean BASDAI scores (n=130) steadily decreased from 3.2 at baseline to 2.8 and 2.5 at 6 and 12 months, respectively, after treatment (ANOVA, p<0.0001). Similarly, overall mean ASDAS ESR (n=130) decreased from 2.7 at baseline to 2.4 and 2.2 af-
ter treatment (ANOVA, p<0.0001). Assessment of disease activity 6 and 12 months after treatment was conducted using the BASDAI scale [Figure 2]. Baseline disease activity scores for NSAIDs ± SSZ treatment patients were lower than the NSAIDs + Etanercept/Infliximab treatment patients (3.02, 2.98, 3.95, and 4.68, respectively). Over time, disease activity decreased across all treatment groups. After 6 months, mean BASDAI scores were lower at 2.65, 2.80, 3.28, and 3.85 for the 4 treatment groups NSAIDs, NSAIDs + SSZ, NSAIDs + Etanercept, and NSAIDs + Infliximab respectively. After 12 months, mean BASDAI scores were further decreased at 2.40, 2.48, 2.86, and 2.97 for the 4 treatment groups NSAIDs, NSAIDs + SSZ, NSAIDs + Etanercept, and NSAIDs + Infliximab respectively. Comparison of mean BASDAI scores, after 12 months of treatment, of patients treated with NSAIDs and patients treated with NSAIDs + SSZ revealed no statistical difference. However, after 12 months of treatment, there was statistically significant difference in mean BASDAI scores of patients treated with NSAIDs vs. patients treated with NSAIDs ± Etanercept (ANOVA, p=0.021). Similarly, after 12 months of treatment, there was statistically significant difference in mean BASDAI scores of patients treated with NSAIDs vs. patients treated with NSAIDs ± Infliximab (ANOVA, p=0.008). Subgroup analysis found statistically significant difference, after 12 months of treatment, in mean BASDAI scores of patients treated with NSAIDs vs. patients treated with NSAIDs + SSZ + Infliximab (ANOVA, p<0.001).

Fig 3: Assessment of disease activity at 6 and 12 months after treatment was also assessed by ASAS ESR scale. Baseline disease activity scores for NSAIDs ± SSZ treatment patients were lower than that in NSAIDs + Etanercept/Infliximab treatment patients (2.64, 2.41, 33.9, and
<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History - Joint disease</td>
<td>5 (3.84)</td>
</tr>
<tr>
<td>Lower back pain (LBA)</td>
<td>102 (78.47)</td>
</tr>
<tr>
<td>Skin Involvement</td>
<td>4 (3.08)</td>
</tr>
<tr>
<td>Ocular Involvement</td>
<td>5 (3.84)</td>
</tr>
<tr>
<td>Peripheral Joint Involvement</td>
<td>56 (43.08)</td>
</tr>
<tr>
<td>Early Morning Stiffness</td>
<td>83 (63.85)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>HLA-B27 positive</td>
<td>93 (71.54)</td>
</tr>
<tr>
<td>X-ray sacroiliac (SI) joint</td>
<td>58 (44.62)</td>
</tr>
<tr>
<td>Magnetic resonance imaging (MRI)</td>
<td>130 (100)</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (ESR), Median</td>
<td>22</td>
</tr>
<tr>
<td>C-reactive protein (CPR)</td>
<td>31 (23.85)</td>
</tr>
<tr>
<td>Disease activity assessment</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>BASMI Score</td>
<td>0.17±0.58</td>
</tr>
<tr>
<td>MASES</td>
<td>0.48±1.01</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.22±1.26</td>
</tr>
<tr>
<td>ASDAS ESR</td>
<td>2.74±0.85</td>
</tr>
</tbody>
</table>

Table 1: Clinical presentation and diagnostic parameters

<table>
<thead>
<tr>
<th>Exam</th>
<th>HLA-B27 Positive</th>
<th>HLA-B27 Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray SI Joint (n=72)</td>
<td>54</td>
<td>18</td>
</tr>
<tr>
<td>Peripheral Joint involvement (56)</td>
<td>40</td>
<td>16</td>
</tr>
<tr>
<td>MRI (n=130)</td>
<td>93</td>
<td>37</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs (n=130)</td>
<td>93</td>
<td>37</td>
</tr>
<tr>
<td>SSZ (n=40)</td>
<td>32</td>
<td>8</td>
</tr>
<tr>
<td>Etanercept (n=13)</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Infliximab (n=17)</td>
<td>14</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2: Correlation between HLA-B27 and other diagnostic and treatment parameters
3.62, respectively). Over time, disease activity decreased across all treatment groups. After 6 months, mean ASDAS ESR scores were lower at 2.21, 2.36, 2.72, and 3.04 for the 4 treatment groups NSAIDs, NSAIDs + SSZ, NSAIDs + Etanercept, and NSAIDs + Infliximab respectively. After 12 months, mean ASDAS ESR scores were further decreased at 2.12, 2.25, 2.26, and 2.65 for the 4 treatment groups NSAIDs, NSAIDs + SSZ, NSAIDs + Etanercept, and NSAIDs + Infliximab respectively. There was statistically significant difference in mean ASDAS scores when comparing patients treated with NSAIDs vs. patients treated with NSAIDs + Infliximab after 12 months of treatment (ANOVA, p<0.0001). Similarly, it was observed that there was statistically significant difference in mean ASDAS scores when comparing patients treated with NSAIDs vs. patients treated with NSAIDs + SSZ after 12 months of treatment (ANCOVA, p<0.001). However, even after 12 months’ treatment, there was no statistically significant difference in mean ASDAS scores when comparing patients treated with NSAIDs vs. patients treated with NSAIDs + Infliximab.

Patient records were also studied to identify the number of HLA-B27 positive patients. Results show that overall 93 (71.5%) patients were HLA-B27 positive. HLA-B27 positive outcome did not completely correlate with other diagnostic exam results [Table 2]. For instance, only 54 of the 72 patients that had X-ray evidence of SI joint involvement were also HLA-B27 positive. Similarly, 40 of the 56 patients who had peripheral joint involvement were HLA-B27 positive. Majority of the patients who had demonstrable disease activity as per the MRI (93 of 130) were HLA-B27 positive.

DISCUSSION

This retrospective study of ASpA patients is a first of its kind from India. The demographics, clinical presentation, and diagnostic features of the studied patient population are similar to previously reported ASpA patient characteristics. Clinically ASpA is spondyloarthropathy with axial skeleton, sacroiliac joints and spine and peripheral joint involvement. In our study, 58% and 56% of the patients were shown to have SI joint and peripheral joint involvement, respectively. In addition, ASpA is accompanied by enthesitis, uveitis, psoriasis, and inflammatory bowel disease which are often treated with SSZ.1 In our study, nearly 31% of patients were treated with SSZ. ASpA is also closely linked to HLA-B27 antigen which was the case for 72% of our patient population. Common symptoms of ASpA such as lower back pain and early morning stiffness were found in over 78% and 64% of our patients, respectively.

The study patients were first treated with NSAIDs which is recommended by ASAR/EULAR as the first-line therapy for ASpA patients. The effect of NSAIDs on disease activity is assessed by several scales including BASDAI and ASDAS.8 We found that a majority of the NSAIDs treated patients (nearly 77%) showed improvements over 12 months. NSAID treatment has been reported to reduce inflammation and improve mobility in ASpA patients.11 In this study, the NSAIDs of choice were indomethacin and etoricoxib. Other NSAIDs used to treat ASpA include diclofenac, ibuprofen, naproxen, celecoxib, and etoricoxib.11

However, some of the patients did not respond to the NSAIDs treatment, with or without SSZ, after 3 months. This subset of the patient population, which had higher baseline disease activity was then additionally treated with anti-TNF-α biologics. It has been reported that patients who received TNF blockers in addition to NSAIDs usually had higher disease activity despite being on NSAIDs therapy.12 This combination treatment strategy was in line with the ASpA management guidelines put forth by ASAR/EULAR which recommends anti-TNF-α blockers as the second-line therapeutic option.13 The criteria for introducing anti-TNF-α treatment include conventional therapy failure or persistently active disease for ≥4 weeks as per the BASDAI index (≥4). Both the anti-TNF-α biologics, etanercept and infliximab, effectively reduced disease activity scores as per 2 different scales. As in our previously published study with ankylosing spondylitis (AS) patients, in this study too we found no statistical difference between etanercept and infliximab treatment effects on reducing disease severity in ASpA patients unresponsive to NSAIDs.

Several other TNF inhibitors such as adalimumab, golimumab, and certolizumab pegol have also been reported to improve ASpA disease activity.11 Other than TNF inhibitors, IL-17 inhibitor, secukinumab is also used as a second-line therapy to treat radiographic ASpA. A meta-analysis by Escalas et al. found that the efficacy of NSAIDs and TNF blockers on patient-reported outcomes was equivalent.12 However, anti-TNF-α biologics are expensive and hence their long-term use may not be affordable for most patients.

In our study we do not have a record of biologics-induced side effects. Research studies have shown that most common side-effects of infliximab include upper respiratory tract infection, nausea, headache, sinusitis, rash, and cough. Etanercept-induced side-effects include erythema, pain, swelling, and itching at the injection site.

In terms of diagnostic exams, all our patients demonstrated disease activity on their MRIs but only 71% of patients were HLA-B27 positive. Rudwaleit et al. discuss in detail the diagnostic algorithm for ASpA in patients who may present with lower back pain. Both, HLA-B27 positivity and sacroiliitis detection via X-ray or MRI scans are highly instrumental in diagnosing and classifying ASpA. However, studies have shown that a subset of patients with X-ray scans detecting sacroiliitis may be HLA-B27 negative.

Future clinical investigations should include larger sample size and investigate the efficacy of anti-TNF-α...
biologics on improving physical function and reducing structural damage\textsuperscript{16}. Poddubny et al. reported a positive link between high disease activity and increasing spine damage in ASpA patients\textsuperscript{17}. Further studies should examine the link between treatment-induced reduction in disease activity as per ASDAS and changes in radiographic evidence of spinal damage.

In summary, results of this study show that all ASpA patients enrolled in this retrospective study demonstrated improvement in disease activity after 12 months of NSAIDs treatment with or without anti-TNF-α biologics. TNF-α inhibitors reduced disease activity in NSAIDs refractory patients, although there was no statistically significant difference in the efficacy—as per mean BASDAI and ASDAS-ESR scores—of etanercept and infliximab treatments.

REFERENCES

Clinical Profile and Treatment of Primary Myelofibrosis - An Observational Study from a Tertiary Care Centre in Kerala, South India


ABSTRACT

Introduction: Primary myelofibrosis (PMF) is a clonal hematopoietic stem-cell disorder, characterized by the abnormal accumulation of mature appearing myeloid cells in the bone marrow. It is one among the primary type of ‘BCR-ABL1 negative’ myeloproliferative neoplasm.

Objectives: The objectives of the study were to describe (i) the Clinical and laboratory profile of Myelofibrosis in Indian patients (ii) to analyze treatment related outcomes of patients receiving Ruxolitinib and Best available therapy (BAT) regimens.

Methods: The study design is an ambivalent cohort. The study period was eight months (September 2015 to April 2016). We collected data through review of clinical records of patients from the hospital information system (HIS). All patients diagnosed as Myelofibrosis and treated in the study institution from January 2010 to April 2016 were included in the study. We identified a total of 76 subjects with a confirmed diagnosis of PMF from the HIS. All identified subjects were included in the final analysis.

Results: The mean age of patients who were on Ruxolitinib was 61.88 ± 10.21yrs and those on BAT was 59.50 ± 11.34 yrs. There were 35 females (Ruxolitinib group=14, BAT group=21) in the study group. Mean MPN score in Ruxolitinib group (n=24) before and after initiation of therapy were 34.46±14.4 and 16.50±16.8 respectively (p-value < 0.001). Mean MPN score in the BAT group (n=22) before and after initiation of therapy were 40.18±19.6 and 27.09±17.06 respectively (p-value < 0.001). A significant improvement in the DIPSS score was seen among Intermediate 2 risk group of the BAT arm (p 0.002) and High risk group of the Ruxolitinib arm (p 0.003). The overall survival function of patients in both the treatment groups was compared using the log rank method and the p-value was found to be 0.333, showing there was no statistically significant difference in survival benefit between the treatment groups.

Conclusion: We found that the clinical profile of PMF patients in our study was similar to the profile described from the western population. There was no significant difference in clinical outcomes as well as survival benefit between the two treatment groups.

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INTRODUCTION

Primary Myelofibrosis (PMF) is a clonal hematopoietic stem-cell disorder, characterized phenotypically by the abnormal accumulation of mature appearing myeloid cells. It is one among the primary type of ‘BCR-ABL1 negative’ myeloproliferative neoplasm. The disease is characterized by the dysregulation of Janus kinase (JAK)–mediated cytokine and growth-factor signal transduction i.e, the JAK-STAT pathway.1

Myelofibrosis (MF) has an incidence of 0.2 per 100,000 persons in United States.2 Published epidemiological data regarding incidence rates for MPN are scarce for Indian population. In a hospital-based study in India among 1814298 patients attended the out-patient department of their institute 231 (0.0127%) were diagnosed as MPN over a period of one year.3

The disease occurs mainly in middle aged and elderly patients and is rare in childhood.4,5 MF is a Ph-ve MPN (Philadelphia chromosome negative Myeloproliferative neoplasm) which is defined by the clinical and pathologic characteristics such as splenomegaly, hepatomegaly, constitutional symptoms, cytopenias and progressive bone marrow fibrosis.6 The constitutional symptoms include weight loss, abdominal pain, abdominal discomfort, dizziness, numbness, insomnia, mood swings, sexuality problems, dyspnoea, low grade fever, cough, impairment in concentration, fatigue, early satiety, night sweats, pruritus, bleeding episodes, diffuse bone pain and impaired quality of life.7 The 2016 revision of the WHO classification of myeloproliferative neoplasm defines 2 stages of PMF: prefibrotic/early (pre-PMF) and overt fibrotic (overt PMF). The fibrotic stage of PMF shows leucoerythroblastic blood picture with the presence of tear drop shaped red blood cells in the peripheral blood smear.8 The overt PMF is enriched with anemia, thrombocytopenia, leucopenia, higher blast count, symptoms, large splenomegaly, and unfavorable karyotype.9 Diagnosis is based on bone marrow morphology. The presence of JAK2, CALR or MPL mutation is supportive but not essential for diagnosis; approximately 90% of patients carry one of these mutations and 10% are “triple-negative”.10 The prognosis of the disease is predicted with two prognostic models (a) International prognostic scoring system -IPSS(at the time of diagnosis) and (b) Dynamic international prognostic scoring system- DIPSS(at any time during the disease course)11.

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Treatment in MF is generally based on the severity of the disease and is often directed to address the individual's clinical features. Pharmacotherapy is generally palliative which is guided by the predominant symptoms derived from anemia, splenomegaly, constitutional symptoms or disease complications due to extramedullary haematopoiesis\(^{12,13,14}\). Current drug therapy in MF is neither curative nor it extents the survival period\(^{15,16}\). The only curative option is allogeneic haemopoietic stem cell transplantation (allo-HSCT) but it carries its own risk of death or chronic morbidity from graft-versus-host disease (GVHD)\(^{17}\). Moreover, it is not a viable option for many MF patients who are advanced in age and/or those with significant co-morbidities. PMF is characterized by significantly reduced overall survival (OS) and increased risk of acute myeloid leukemia (AML) progression\(^{18}\). The median survival is estimated as 6.5years (range of 2-10years)\(^{19}\).

Absence of a well-defined cancer registry for these neoplasms and unavailability of molecular diagnosis to many clinicians are the two major challenges in determining the incidence of the disease in our country\(^1\). There exists scarcity in data regarding the clinical profile, diagnosis and treatment of MF in Indian population. Our study attempts to bridge these existing gaps.

**MATERIALS AND METHODS**

The current study is an ambivalent cohort study carried out for a period of eight months (1st September 2015 to 30th April 2016) in the haematology department of a tertiary care centre in South India. Patients diagnosed as MPN (n=76) under all age groups during the period of 1st January 2010 till 31st May 2016 were selected for the study. Patients with secondary Myelofibrosis (tuberculosis, myeloma, chronic myeloid leukemia, acute myeloid leukemia, hairy cell leukemia) and MPN without a marrow fibrosis were excluded from the study. The seventy six patients were divided into two groups- (a) patients under Ruxolitinib therapy (n=34) and (b) patients under BAT (n=42).

A standardized data collection form was used to collect all the necessary information of the study participants required for the study. The Myelofibrosis symptom assessment form (MSAF) was used to measure the symptoms\(^{20,21,22}\). The MPN score was assessed before (at diagnosis) and after (best response during follow up) the initiation of therapy.

The Drug Related Problems were identified by reviewing the Hospital’s Health Information System and classified according to the PCNE (Pharmaceutical Care Network Europe) version V\(^6\). Using this, the problem was categorized; causes identified and appropriate intervention was provided. The interventions were conveyed to the patient after physician’s acceptance. The outcome of these interventions was assessed during the patient’s follow up visit. The drug interactions were checked using Lexicomp Drug interaction checker. ADR was assessed using Naranjo Adverse Drug Reaction Probability Scale\(^{23}\). Using IPSS and DIPSS prognostic scales the prognosis of the disease was calculated\(^{11}\).

**Statistical analysis**

The data collected were compiled using Microsoft Excel. All statistical analyses were carried out using IBM Statistical Package for Social Science (SPSS version 20). We used frequency and percentage to present categorical variables and mean and standard deviation to present numerical variables. Chi-square test was used to examine the association between categorical variables. Independent two sample T-test and Mann-Whitney U-test were used for parametric and non-parametric data comparisons respectively. Kaplan Meier Test was used to obtain the survival probability. Log Rank test was used to compare the survival outcome between the two treatment groups.

**RESULTS**

Among study patients, a total of 45 patients (59.21%) were under <65 years of age (18 in the 34 of Ruxolitinib group and 27 in the 42 of BAT group). There were 31 patients (40.78%) (16 under Ruxolitinib group and 15 under BAT group) aged>65 years. The mean age of patients who were on Ruxolitinib was 61.88 ± 10.21 and those on BAT was 59.50 ± 11.34. There were 35 females (14 in the Ruxolitinib group and 21 in the BAT group) in the study. Among patients, only 60 had reticulin score in which 17 (28.33%) had a reticulin score< 3 and 43 (71.66%) had a score of≥ 3. Among the 34 patients in the Ruxolitinib group, 35.7% (n=10) had a reticulin score of less than 3 and 64.3% (n=18) had score ≥3. In 42 patients in the BAT arm, 21.9% (n=7) had a score of less than 3 and 78.1% (n=25) had a score ≥3. FISH analysis was done in both groups. In the Ruxolitinib group (n=26) 25 patients were BCR ABL-ve. Among the patients who were on BAT group (n=22) all were BCR ABL-ve.JAK2 mutation was done in both groups. In the Ruxolitinib arm, 23 patients had done JAK2 mutation in which 16 (69.56%) patients were identified with JAK2-+ve mutation. In patients who were on BAT, 15 had done JAK2 mutation and among them 7 (46.66%) patients were JAK2-+ve.

The laboratory values for haemoglobin, WBC count, platelet count and LDH at diagnosis were collected. The mean Hb (g/dl) in Ruxolitinib group was 10.95±5.25 and in BAT group was 9.70±3.19. The mean WBC (K/uL) in Ruxolitinib group was 18.12±17.43 and in BAT group was 16.29±18.57. The mean PLT (K/uL) in Ruxolitinib group was 264.74±281.32 and in BAT group was 333.37±321.48. The mean LDH (U/L) in Ruxolitinib group was 556.33±247.17 and in BAT group was 515.70±381.28 (Fig1).

**Treatment profile**

Our study population consisted of patients who were on 2 different treatments in which 42 were on BAT — 18 received hydroxyurea and prednisolone, 17 received...
Clinical Profile and Treatment of Primary Myelofibrosis - An Observational Study from a Tertiary Care Centre in Kerala, South India

Fig 1: Laboratory values at diagnosis of PMF patients

Fig 2: IPSS & DIPSS risk categorization of BAT and Ruxolitinib
A significant improvement in the DIPSS score was seen among Intermediate 2 risk group of the BAT arm \( (p < 0.002) \) and High risk group of the Ruxolitinib arm \( (p < 0.003) \).

Adverse drug reactions (ADR)

The most commonly reported ADR was grade 3 thrombocytopenia in both groups. The occurrence of ADR was observed in most patients who were on Ruxolitinib. These ADRs were managed by interim dose changes and temporary discontinuation of therapy.

Survival analysis in each group

The overall survival function of patients in both the treatment groups was compared. There was no statistically significant difference in survival benefit between the treatment groups \( (p = 0.333) \). The details are presented in Table 1.

### Table 1: Survival analysis in each group

<table>
<thead>
<tr>
<th>Groups</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Ruxolitinib</td>
<td>1466.875</td>
<td>170.337</td>
<td>1133.014</td>
<td>1800.735</td>
<td></td>
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<tr>
<td>BAT</td>
<td>1342.772</td>
<td>142.590</td>
<td>1063.295</td>
<td>1622.249</td>
<td>0.333</td>
</tr>
<tr>
<td>Overall</td>
<td>1461.302</td>
<td>112.856</td>
<td>1240.104</td>
<td>1682.500</td>
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</table>

**DISCUSSION**

PMF is the rarest condition among all MPNs and is the most obscure with regards to pathophysiology. During our study, we screened out 76 patients with MF from 7289 bone marrow aspiration reports. We tried to identify the patterns of treatment in this condition. Traditionally available treatments were hydroxyurea, thalidomide with/without prednisolone, lenalidomide with/without prednisolone, radiotherapy and splenectomy. Studies conducted by Trillos A M et al\(^a\), Thapaliya P et al\(^a\), Quintas-C A et al\(^a\), had proved the efficacy and tolerability of these treatments in MF patients. We also had patients on newer therapy like the JAK1/2 inhibitor, Ruxolitinib. Ruxolitinib first of its kind to gain approval by the FDA on November 16, 2011 for the treatment of MF in intermediate-2 and high risk patients. It was also
approved for the treatment of post-PV MF and post-ET MF 26. In our study, we segregated patients into two groups: one group with patients on Ruxolitinib (n=34) and the other arm on traditional therapy (BAT) (n=42). Demographic profiles of these patients were observed and the pattern of distribution in age, gender and JAK2 mutation were seen. In our study, majority of patients were under the age group of less than 65 years i.e. 59.2% and greater percentage were male patients i.e. 53.9%. These data were similar to a study by Keith L D et al with 84.26% under the age group of less than 65 years and 66.7% were male patients 20. Similarly in the distribution of JAK2 mutation, greater proportion was seen with JAK2 +ve mutation i.e. 60.5% which was consistent with those reported in the study by Keith et al (68.5%).

The prognostic models used to calculate the survival probability were IPSS and DIPSS. The percentage of patients in IPSS low-risks were 8%, IPSS intermediate-1 were 28%, IPSS intermediate-2 were 30.67% and IPSS high risk were 33.33%. These findings were similar to that of the study conducted by Gangatet a 12. According to the DIPSS calculation, the percentage of patients under low risk were 10.6%, intermediate-1 were 39.4%, intermediate-2 were 33.3% and high risk were 16.7%. Our findings are similar to the study conducted by Gangatet al. In our study there was a 67.7% and 37.10% improvement in life expectancy in patients receiving Ruxolitinib and BAT respectively which was assessed through the improvement in the DIPSS score 11.

The number of patients who received hydroxyurea was 35, thalidomide-prednisolone was 26, lenalidomide-prednisolone was 4 and danazol were 7 and prednisolone alone was 15. Out of this, 27 switched over to Ruxolitinib due to inadequate improvement in MF-related symptoms. The number of patients who were initiated directly on Ruxolitinib was 7. In our study, we tried to assess the clinical outcome of Ruxolitinib and BAT based on the MPN score. Constitutional symptom improvement was assessed through MPN scoring system, taken at two time points- before and after initiation of each therapy. In general, in both treatment groups a distinct shift was observed in the distribution of symptom severity towards a more favourable profile (i.e., less severe) from MF diagnosis to the time of best response.

We noticed an improvement in all the 10 symptoms out of which weight loss (13 patients), fatigue (5 patients), early satiety (6 patients), abdominal discomfort (6 patients), problems with concentration (5 patients) and night sweats (5 patients) were the most significantly resolved ones. There was no significant difference in the mean decline in MPN score from base line to follow up between both groups.

We also examined the safety profile of the patients in both treatment groups. There were both haematological and non-haematological adverse events. A total of 29 adverse events occurred in 16 patients taking Ruxolitinib (85.29%) and 30 adverse events in the BAT arm (71.42%). Greater number of ADRs was reported in the Ruxolitinib arm. The most commonly observed ADR was thrombocytopenia which was predominantly grade III.
A similar pattern in the occurrence of adverse events was shown in the COMFORT-II trial. These haematological events were reversible, so close monitoring of haematological parameters is needed. Due to these ADRs, 16 patients were managed by interim dose changes and temporary discontinuation of Ruxolitinib therapy. Discontinuation of therapy was seen only in 1 patient due to loss of response as the patient was on sub optimal dose of Ruxolitinib therapy.

The mortality in the Ruxolitinib and BAT group were 14.7% and 21.4% respectively. Transformation to AML occurred in 5 patients in this study; one from BAT arm and 4 from ruxolitinib arm. A study done by Verstovsek S et al had reported 2 cases of transformation to AML.

CONCLUSION

We found that the clinical profile of PMF patients was similar to that of western population. There was no significant difference in clinical outcome as well as survival benefit between the two treatment groups.

Limitations

The main limitation of our study is the retrospective nature of design. Lack of documentation probably affected our data quality to some extent since we were dependent mostly on electronic databases for extraction of data. Karyotyping could not be done in a subset due to insufficient facilities and/or poor financial resources of patients. Approximately half of our patients were on sub-optimal dose in Ruxolitinib group due to financial constraints. This could probably have decreased the complete targeted action of Ruxolitinib.

REFERENCES

25. Lofvenberg E & Wahlin A. Management of Polycythemia vera, es-


Need of Routine Upper GI Endoscopy in Renal Transplant Workup Patients in a Resource Limited Setting- A Cross Sectional Study from Kerala, South India

Vijay Anand Viswanathen*, Govind Vijayakumar**, Remya Sudevan***

ABSTRACT

Background: Patients with chronic renal failure (CRF) often have dyspeptic symptoms and may develop peptic diseases. The possibility of these may be aggravated by use of immunosuppression during post transplant. Development of gastrointestinal complications including GI bleed can be devastating in the post transplant period.

Objectives: To evaluate the diversity of gastrointestinal symptoms, upper gastrointestinal endoscopic findings and prevalence of Helicobacter pylori infection in patients with CRF undergoing transplant workup.  

Methodology: This cross sectional study was conducted for a period of 20 months (April 2013 - November 2014) in the gastro department of a tertiary care centre. Sixty nine consecutive patients with chronic renal failure, dialysis dependant, who were being worked up for transplant were enrolled in the study. All patients completed a standardized questionnaire scoring the presence of various GI symptoms and underwent upper GI endoscopy with multiple biopsies sampling for histopathological examination and H pylori identification.

Results: Mean age of the study participants was 40.2 ±5.7 years. There were 51 males in the study. Only 21(30 %) of the patients were symptomatic. The most common symptoms seen were dyspepsia, black stools, abdominal pain and anorexia. Abnormal endoscopic findings were seen in 62(89.9%) of patients. Among 21 symptomatic patients, 18(85.7%) had abnormal OGD findings. In the 48 asymptomatic patients, 44 (91.7%) had abnormal OGD findings. In the total of 69 patients only 20 (29%) had H pylori infection. In the normal OGD group of seven, five patients (71.4%) were positive for H pylori. In the abnormal OGD group of 44, only 15 patients (31.9%) were positive for H pylori.

Conclusion: Patients with Chronic renal failure have a low frequency of GI symptoms, contrary to expectations. Even in asymptomatic patients, the occurrence of abnormal OGD findings is very high. Pre transplant OGD may help in assessing these lesions and prevent complications during post transplant period. Routine upper gastrointestinal endoscopy and testing for H pylori may have to be considered in Chronic renal failure patients as part of transplant workup.

Corresponding Author: Remya Sudevan

INTRODUCTION

Chronic Kidney Disease (CKD) patients receiving haemodialysis treatment frequently experience dyspeptic symptoms such as nausea, vomiting, abdominal distension, early satiety, and anorexia. Uraemia and dialysis are found to be the risk factors for developing these symptoms as well as lesions in the gastrointestinal tract for CKD patients. All patients with CKD can have extensive gastritis. The gastritis will be asymptomatic unless the patient had oesophagitis or a well established peptic ulcer. Another factor that contributes in the increased rate of GI complaints in CKD patients is Helicobacter pylori infection rate. These GI complaints can get aggravated and become fatal during post transplant period due to immunosuppression. Our study aims to examine the various GI symptoms, endoscopic findings and H pylori infection rate of patients with CKD who had been worked up for renal transplantation.

METHODS

The study was cross sectional in design and was conducted in the gastro department of a tertiary care center. The study period was 20 months (April 2013 to November 2014). The study subjects were CKD patients under dialysis who were undergoing workup for renal transplant. Inclusion criteria were all adult patients who had attended the gastroenterology clinic with diagnosis of CKD for pre transplant workup and on regular haemodialysis for a minimum of 6 months before the study. All patients with a history of smoking, alcohol abuse and malignancy were excluded. Patients with history of peptic ulcer disease, or upper GI bleed and patients who had received antibiotic or antacid or H2 receptor inhibitor therapy during the past 3 months before study were also excluded from the study. A total of 69 CKD patients who satisfied the inclusion and exclusion criteria were consecutively enrolled for the study. All patients were examined by the gastroenterologist and GI symptoms were evaluated using a questionnaire scoring GI symptoms. The endoscopic procedure was performed on a non-dialysis day by the principal investigator. Patients were considered endoscopically normal if no mucosal abnormalities were found. Ulcers were diagnosed when mucosal denuding was over 5mm in diameter. Multiple gastric antral biopsies were obtained from an intact mucosa in the antrum within 5 cm of the pylorus, fixed.
in 10% formalin and sent for histopathological examination and Helicobacter pylori identification for all the enrolled patients. The study was approved by the ethical committee of the institution and informed written consent was obtained from all the patients included in the study. Data was collected using a standardized proforma and analyzed using Statistical Package for Social Science (SPSS) version 19.0 statistical software. All continuous variables are expressed as mean (SD) and frequency in percentage.

RESULTS

A total of 69 patients were included in the study. The mean age of the patients in the study was 40.2 ± 5.7 yrs. Among study subjects 51 (73.9%) were male. Among study subjects 48 (70%) were found to be asymptomatic. The distribution of symptoms were dyspepsia for 8 patients, black stools for 6, abdominal pain for 6, anorexia for 6, nausea for 5, anemia for 3 and dysphagia for 2. Normal findings in OGD were seen in seven patients (10%). Abnormal endoscopic findings were seen in 62 patients (89.9%). The most prevalent abnormal findings were antral erosions in 19 (31%), antral gastritis in 18 (29%), reflux esophagitis in 12 (19%), duodenal erosions in 11 (18%), Pangastritis in 8 (13%) and duodenal ulcer in 5 (8%). The diversity of distribution of abnormal endoscopic findings observed in oesophago-gastro-duodenoscopy (OGD scope) is shown in table 1.

In the 21 symptomatic patients, 18 (85.7%) had abnormal OGD findings and three had normal OGD findings. In the 48 asymptomatic patients, 44 (91.7%) had abnormal OGD findings. Only 4 asymptomatic patients had normal OGD findings. Fig 1

In the total of 69 patients, 20 (29%) had H pylori infection and the rest were H pylori negative. In the normal OGD group of seven patients, five patients (71.4%) were positive for H pylori. In the abnormal OGD group of 62 patients, 15 patients (31.9%) were positive for H pylori. The comparison of H pylori infection between normal OGD and abnormal OGD groups is shown in Fig 2.
the study by Dong et al and nausea. This symptom profile is in agreement with were dyspepsia, black stools, abdominal pain, anorexia of time. The study showed that the frequent symptoms complications and H pylori infection at a single point which measured the GI symptoms, who have gastro-intestinal complaints and mortality are often more in this group of patients removed by dialysis. Due to these reasons, morbidity and mortality are often more in this group of patients who have gastro-intestinal complaints. Our study was a cross sectional one which measured the GI symptoms, complications and H pylori infection at a single point of time. The study showed that the frequent symptoms were dyspepsia, black stools, abdominal pain, anorexia and nausea. This symptom profile is in agreement with the study by Dong et al. The most frequently observed endoscopic findings were antral erosions (31%), antral gastritis (29%), reflux esophagitis (19%), duodenal erosions (18%), Pangastritis (13%) and duodenal ulcer (8%). The results were similar to that reported by Krishnan et al. H pylori infection was positive in 71.4% of patients who had normal OGD scoppy findings. In abnormal OGD scopy group only 31.9% of patients were H pylori positive. Nakajima et al reported similar findings in their study. The reason they suggested for the lower prevalence of H pylori in long term dialysis patients was reduction of gastric acid secretion related to chronic gastritis. A study done by Sugimoto et al concluded that the prevalence of H pylori infection is similar in individuals with normal renal function and that of patients under haemodialysis for less than 1 year. All these studies suggest that haemodialysis treatment per se is responsible for the lower prevalence of H pylori infection and not by the background uraemia alone.

CONCLUSIONS
Our study suggests that the majority of the patients with CKD on dialysis were asymptomatic from a gastrointestinal perspective. Abnormal endoscopic findings were shown by majority of the study subjects. H pylori infection was seen in one out of three patients and was more in the asymptomatic group. All these observations suggest pre transplant OGD may help in assessing the abnormal GI lesions and the same can lead to reduction in post-transplant complications. We conclude that routine upper gastrointestinal endoscopy and testing for H pylori infection may have to be considered in chronic renal failure patients as part of a complete renal transplant workup.

REFERENCES

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<th>Type of abnormal condition</th>
<th>Number</th>
<th>Percentage (%)</th>
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</thead>
<tbody>
<tr>
<td>Antral erosions</td>
<td>19</td>
<td>31</td>
</tr>
<tr>
<td>Antral gastritis</td>
<td>18</td>
<td>29</td>
</tr>
<tr>
<td>Reflux esophagitis</td>
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<td>19</td>
</tr>
<tr>
<td>Duodenal erosions</td>
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<td>18</td>
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<tr>
<td>Pangastritis</td>
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<td>13</td>
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<tr>
<td>Duodenal ulcer</td>
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<td>8</td>
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<tr>
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<td>2</td>
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<tr>
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<td>2</td>
</tr>
<tr>
<td>Duodenal ulcer with active bleed</td>
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<td>2</td>
</tr>
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</table>

Table 1: Distribution of abnormal OGD findings

DISCUSSION
In developing countries gastrointestinal complaints are more prevalent in patients with renal diseases probably due to poor resources and inadequate care. The incidence of GI symptoms varies from 37% to 93%. The main risk factors for this increased occurrence are uraemia and dialysis. The mechanisms by which uraemia causing frequent GI symptoms are disequilibrium of liquid and electrolytes, mechanical, physical and emotional problems of patients and toxins which cannot be removed by dialysis. Due to these reasons, morbidity and mortality are often more in this group of patients who have gastro-intestinal complaints. Our study was a cross sectional one which measured the GI symptoms, complications and H pylori infection at a single point of time. All these studies suggested pre transplant OGD may help in assessing the abnormal GI lesions and the same can lead to reduction in post-transplant complications. We conclude that routine upper gastrointestinal endoscopy and testing for H pylori infection may have to be considered in chronic renal failure patients as part of a complete renal transplant workup.
Comparision of APACHE 2 vs SOFA Scores in Predicting Mortality Among Patients in ICU

Rema pai*, Pillai MGK*, Mohanakkannan S*

ABSTRACT

Background: SOFA and APACHE2 are two scoring systems which are being used in the ICU to predict mortality among patients in ICU. The question which among these systems is better remains elusive.

Objective: Goal of this study is to compare the ability of SOFA (Sequential organ failure assessment) and Acute physiology and chronic health evaluation (APACHE) II scoring system to predict mortality and morbidity in ICU patients.

Methods: Prospective observational study of 74 patients who were admitted in the ICU from January 2014 to December 2014, a period of one year was done. The scoring systems of SOFA and APACHE2 were done on the admitted patients on day 1 of the admission.

Results: There were totally 46 patients in the alive group of which 16(33%) were female and 30(67%) were male. The mean age was 60 years. The SOFA scores of patients less than 60 years of age was compared with the SOFA scores of patients more than 60 years of age but there was no significant difference between them. The APACHE scores of patients less than 60 years of age was compared with the SOFA scores of the patients more than 60 years of age and there was no significant difference showed that SOFA was a better predictor of mortality than the APACHE scores (p = 0.048). Comparison of APACHE and SOFA scores on the basis of length of ICU stay shows that APACHE is a better predictor of the morbidity (length of stay in ICU) than the SOFA scores. P values are significant (<0.001 for APACHE as compared to 0.287 for SOFA)

Conclusion: Our study showed that SOFA scores were a better predictor of mortality among ICU patients when compared with APACHE2, hence SOFA scoring can be considered in ICU patients for triaging and to look for treatment outcomes.

Corresponding Author: Rema pai

INTRODUCTION

Scoring systems in ICU have been in use since the past 35 years and they help in the assessment of a critically ill patient. There are different types of scoring systems and they can be broadly classified into scores that measure the severity of the disease by various physiological parameters at the time of admission (APACHE), Simplified Acute Physiology Score (SAPS), Mortality Probability Model (MPM)), scores that assess the presence and severity of organ dysfunction Multiple Organ Dysfunction Score (MODS), Sequential Organ Failure Assessment (SOFA), and scores which assess nursing workload use (for example, Therapeutic Intervention Scoring System (TISS), Nine Equivalents of Nursing Manpower Use Score (NEMS). Other than triaging, comparative audit, scoring systems have a lot of proposed roles in clinical management of patients. The first ICU model of disease severity, The Therapeutic Intervention Scoring system (TISS), was proposed in 1974.

The Sequential Organ Failure Assessment score, or just SOFA score, is used to track a patient’s status during the stay in an intensive care unit (ICU). Sequential readings are done at 0 – 24 hours, and then after 48 hours. Six organ systems (respiratory, cardiovascular, renal, hepatic, central nervous, coagulation) were selected based on a review of literature, and function of each one is scored from 0 (normal function) to 4 (most abnormal), giving a possible score from 0 to 24. APACHE II (“Acute Physiology and Chronic Health Evaluation II”) is a severity-of-disease classification system, one of several ICU scoring system. It is applied within 24 hours of admission of a patient to intensive care unit (ICU). Higher scores correspond to more severe disease and a higher risk of death. In APACHE II, there are just 12 physiological variables, compared to 34 in the original score. The effects of age and chronic health status are incorporated directly into the model, weighted according to their relative impact, to give a single score with a maximum of 71. The worst value recorded during the first 24 hours of a patient’s admission to the ICU is used for each physiological variable.

METHODS AND MATERIALS

Ours was a prospective study over a period of one year [2013-2014] and patients are enrolled as per inclusion criteria. Sample size was set to be a minimum of 80. Patients admitted to AIMS [Amrita Institute of Medical Sciences] a tertiary care hospital in intensive care unit under internal medicine during study period were taken for study when they come under inclusion criteria. The physiological parameters, lab investigations, surgical status, chronic health condition including the demographic details as needed by scoring systems [APACHE II, SOFA] were recorded at the time of admission to ICU. No changes were made in treatment protocol of study patients. The treating physician/emergency medicine team in charge of ICU and staffs was unaware, that patients are enrolled into the study. This is to avoid

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any bias into the primary end point of study. The study patients were given the same care as provided to all patients. Patients were followed up till the time of discharge and mortality among the study patients were documented.

All patients above the age of 17 who were admitted to ICU under internal medicine with a minimum ICU stays of twenty four hours were included. Patients less than 17 years were excluded and patients from outside hospital ICU were excluded due to lead time bias. Based on the results of the iSOFA and APCACHE 2 scores with respect to mortality (references- Dino Adrian Halim et al2) and with 95 % confidence and 80 % power minimum sample size comes to 48 survivors and 26 non survivors. The scores were calculated for study patients according to the scoring systems studied(APACHE II, SOFA). APACHE II and SOFA scores were calculated using online calculators from Globalrph web portal. Also predicted mortality by each scoring systems have been documented and analyzed statistically to meet the objective of study.

Statistical analysis is done by using SPSS software Wilcoxon signed Rank test was used to compare mean scores of APACHE and SOFA. Mann Whitney U test was used to compare mean scores within APACHE and within SOFA (between mortality, age, length of ICU stay). Mann Whitney U Test was used to compare mortality between SOFA and APACHE 2 scores.

RESULTS

62.2% (46) of the total study population was of male sex and 37.8% (28) of the study population was female sex. 39.2% of the total study population was under the age of 60 years and 60.8 % of the study population was above the age of 60 years. Of all the cases which were studied the maximum number of cases were involving multi organ system (24.3%), followed by gastroenterology (20.3%) and then by neurology (18.9%). The other cases involved pulmonary medicine (16.2%), Hemat/Oncology (9.5%), cardiology (8.1%) and nephrology (2.7%).

The number of patients in the study who were admitted in the ICU for less than 5 days were 39.2% and the percentage of patients who were admitted in the ICU for more than 5 days was 21.6%. The SOFA scores of patients less than 60 years of age was compared with the SOFA scores of patients more than 60 years of age but there was no significant difference between them. The APACHE scores of patients less than 60 years of age was compared with the SOFA scores of patients more than 60 years of age but there was no significant difference between them. The SOFA scores were compared between males and females and there was no significant differences in prediction of mortality/morbidity. The APACHE scores were compared between males and females but there was no significant differences in prediction of mortality/morbidity.
**DISCUSSION**

Comparison of APACHE and SOFA scores on the basis of length of ICU stay shows that APACHE is a better predictor of the morbidity (length of stay in ICU) than the SOFA scores. P values are significant (<0.001 for APACHE as compared to 0.287 for SOFA).

Comparison of SOFA and APACHE 2 scores on the basis of mortality of the patients showed that SOFA was a better predictor of mortality than the APACHE scores (p=0.048).

Our study gives the same final conclusion as the study done by Dino Adrian Halim, Tri Wahyu Murni, Ike Sri Redjeki et al. which also went on to show that SOFA scores were better than APACHE scores in predicting the mortality among ICU patients, but differs from the other study done by Hwang et al. which said that SOFA scores were equivalent to APACHE scores.

**CONCLUSION**

The study goes on to show that SOFA scores are better predictor of the mortality among ICU patients and APACHE scores are a better predictor of morbidity (Length of stay in ICU) among ICU patients. It would be prudent to consider SOFA scores better than the APACHE scores since mortality is better predicted by it and patients with very high SOFA scores should be taken as those with very high risk for mortality and should be treated accordingly.

**REFERENCES**

1. Severity scoring systems in the critically ill D. Christopher Bouch, MB ChB FRCA EDIC Jonathan P. Thompson, BSc (Hons) MB ChB MD FRCA
2. Clinical review: Scoring systems in the critically ill Jean-Louis Vincent1* and Rui Moreno2 * Corresponding author: Jean-Louis Vincent jlvincen@ulb.ac.be Author Affiliations, 1. Department of Intensive Care, Erasme University Hospital, Route de Lennik 808, 1070 Brussels, Belgium, 2. Department of Intensive Care, Hospital de St Antonio dos Capuchos, Centro Hospitalar de Lisboa Central, EPE, 1169-050 Lisbon, Portugal
3. Kevin Gunning, Kathy rpwan ABC of intensive care, BMJ vol319
5. Clinical review: Scoring systems in the critically ill Jean-Louis Vincent* and Rui Moreno
6. Comparison of the Sequential Organ Failure Assessment, Acute Physiology and Chronic Health Evaluation II scoring system, and Trauma and Injury Severity Score for predicting the outcomes of intensive care unit trauma patients Seong Youn Hwang, Jun Ho Lee, Young Hwan Lee, Chong Kun Hong
7. Comparison of Apache II, SOFA, and Modified SOFA Scores in Predicting Mortality of Surgical Patients in Intensive Care Unit at Dr. Hasan Sadikin General Hospital Dino Adrian Halim, Tri Wahyu Murni, Ike Sri Redjeki

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**Comparison of APACHE vs SOFA scores on the basis of length of ICU stay**

<table>
<thead>
<tr>
<th>Method</th>
<th>No of ICU stay</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>p value</th>
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<td>SOFA</td>
<td>Less than 5 days</td>
<td>29</td>
<td>.081</td>
<td>.083</td>
<td>.287</td>
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<tr>
<td></td>
<td>Greater than 5 days</td>
<td>16</td>
<td>.106</td>
<td>.107</td>
<td></td>
</tr>
<tr>
<td>APACHE 2</td>
<td>Less than 5 days</td>
<td>29</td>
<td>.164</td>
<td>.105</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Greater than 5 days</td>
<td>16</td>
<td>.333</td>
<td>.171</td>
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30
Lipid Profile in Executive Health Checkup Patients in a Tertiary Health Care Center in Kerala

Dayana Antony*, Nisha Bhavani*

ABSTRACT

Literature regarding prevalence of dyslipidemia in this part of the world is very scarce. This study was aimed at studying the fasting lipid profile of a cohort of patients attending the executive health check up program of a tertiary care centre in central Kerala. 200 patients with no past history of dyslipidemia and who are not on any lipid modifying drugs had their fasting lipid profile done after 14 hours overnight fasting. Mean of lipid parameters in the total population was Total cholesterol- 232.mg/dl Triglyceride- 172.mg/dl HDL-43.49mg/dl and LDL- 158.86mg/dl. Only 10-11% of population had normal Total cholesterol and LDL levels whereas normal triglyceride and HDL were seen in 44 % and 36.5% respectively. The prevalence of dyslipidemia was markedly higher compared to other population. There was no significant difference in the prevalence of dyslipidemia between diabetic and non-diabetics.

Corresponding Author: Nisha Bhavani

INTRODUCTION

Along with Type 2 Diabetes Mellitus, dyslipidemia has become a common disorder in the present day world. Both disorders along with systemic hypertension, obesity and insulin resistance contribute to the metabolic syndrome which significantly increases the risk of cardiovascular disease.

The prevalence of dyslipidemia varies in different population. South Asians are reported to have a high incidence of metabolic syndrome1,2. Data regarding the prevalence of dyslipidemia in (our local) population is scanty. So we aimed to study the prevalence of lipid disorders in a cohort of patients attending the executive health care clinic of a tertiary health care center. We also aimed to study the difference in lipid profile in patients with characters known to affect lipid profile like age, gender, BMI and presence and absence of diabetes.

METHODS

A cross-sectional study was conducted, among 200 patients attending the Comprehensive Health clinic of a tertiary referral center. All patients above the age of 20yrs were included. Patients who are on treatment for dyslipidemia or with past history of dyslipidemia or those with comorbidities affecting lipid profile like renal failure, nephrotic syndrome and hypothyroidism were excluded from the study.

Fasting lipid profile was done in all patients after 14 hours fasting by Photometric enzymatic method. Dyslipidemia was diagnosed according to ATP and NCEP guidelines shown below. Patients were classified according to their age, BMI, sex, and presence or absence of diabetes into different categories. Statistical analysis was done using SPPS version. Categorical variables were compared using Chi-square test.

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<th>Lipid</th>
<th>Normal lipid levels (mg/dl) (NR)</th>
<th>Borderline risk lipid levels (mg/dl) (BR)</th>
<th>High Risk lipid levels (mg/dl) (HR)</th>
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<td>LDL</td>
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<tr>
<td>Triglyceride</td>
<td>&lt;150</td>
<td>150-200</td>
<td>&gt;200</td>
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</table>

Table 1: ATP and NCEP classification

*Dept. of Endocrinology, AIMS, Amrita Vishwa Vidyapeetham, Kochi, India.
RESULTS
Results are tabulated in the tables given below

<table>
<thead>
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<th>Characteristics</th>
<th>Categories</th>
<th>Frequency</th>
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<tbody>
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<td>Young age (YA)</td>
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<td>Female(FM)</td>
<td>122</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (NW)</td>
<td>&lt;23.5</td>
<td>43</td>
<td>21</td>
</tr>
<tr>
<td>Overweight(OW)</td>
<td>23.5-27.5</td>
<td>70</td>
<td>35</td>
</tr>
<tr>
<td>Obese(OBW)</td>
<td>&gt;27.5</td>
<td>73</td>
<td>34</td>
</tr>
<tr>
<td>Type 2 Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes(DM)</td>
<td>100</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>No (NDM)</td>
<td>100</td>
<td>50</td>
<td></td>
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Table 2: Number of cases in each category

<table>
<thead>
<tr>
<th>TOTAL</th>
<th>YA</th>
<th>MA</th>
<th>OA</th>
<th>FM</th>
<th>M</th>
<th>NW</th>
<th>OW</th>
<th>OBW</th>
<th>DM</th>
<th>NDM</th>
</tr>
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<tbody>
<tr>
<td>TC</td>
<td>232</td>
<td>226</td>
<td>234</td>
<td>231</td>
<td>236</td>
<td>229</td>
<td>230</td>
<td>228</td>
<td>238</td>
<td>230</td>
</tr>
<tr>
<td>TG</td>
<td>172</td>
<td>176</td>
<td>175</td>
<td>158</td>
<td>141</td>
<td>192</td>
<td>155</td>
<td>193</td>
<td>166</td>
<td>168</td>
</tr>
<tr>
<td>HDL</td>
<td>43</td>
<td>40</td>
<td>44</td>
<td>45</td>
<td>45</td>
<td>42</td>
<td>43</td>
<td>42</td>
<td>43</td>
<td>42</td>
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<tr>
<td>LDL</td>
<td>158</td>
<td>156</td>
<td>160</td>
<td>156</td>
<td>162</td>
<td>156</td>
<td>160</td>
<td>154</td>
<td>162</td>
<td>155</td>
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</tbody>
</table>

Table 3: Correlation between PCT max and organisms isolated

<table>
<thead>
<tr>
<th>%</th>
<th>TG&gt;150 &amp; HDL&lt;35</th>
<th>LDL&lt;100</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
<td>13.5</td>
<td>1.5</td>
</tr>
<tr>
<td>DM</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>NDM</td>
<td>15</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 4: Percentage Prevalence of dyslipidemia in diabetics and nondiabetics
Lipid parameters were similar in most groups except for a significantly higher triglyceride level in males vs females (p<0.01), higher total cholesterol in obese vs overweight (p<0.03), and higher TG in normal vs overweight vs obese (p<0.01 and 0.03 respectively). The HDL levels were significantly lower in young age vs other age groups. (YA vs MA p<0.03 and YA vs OA p<0.02) Lipid parameters were similar in diabetics and nondiabetics. The classic diabetic lipid profile of high TG and low HDL were similar in diabetic and nondiabetics. A diabetic target LDL < 100 was present only in 1% of diabetics and 2% of nondiabetics.

<table>
<thead>
<tr>
<th>Lipid Profile</th>
<th>Normal Risk NR</th>
<th>Borderline Risk BR</th>
<th>High Risk HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>23 (11.5%)</td>
<td>103(51.5%)</td>
<td>74(37.7%)</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>88(44.3%)</td>
<td>48(24.9%)</td>
<td>64(32.0%)</td>
</tr>
<tr>
<td>HDL</td>
<td>73(36.5%)</td>
<td>96(48.8%)</td>
<td>31(15.5%)</td>
</tr>
<tr>
<td>LDL</td>
<td>21(10.5%)</td>
<td>86(43.4%)</td>
<td>93(46.5%)</td>
</tr>
</tbody>
</table>

Table 5: Dyslipidemia risk profile in the total population. N (%)
In females, majority had borderline risk TC levels, high risk LDL levels and normal TG and HDL levels. In males, majority had high risk TG levels, normal LDL levels and borderline risk TC and HDL levels. In non-diabetics, majority had borderline risk TC, LDL and HDL levels and normal TG levels. In diabetic, majority had high risk LDL levels, borderline risk TC levels and normal TG and HDL levels. In normal BMI groups, majority had borderline risk TC and HDL levels and normal TG levels. In young age, majority had borderline risk TC and HDL levels and normal TG levels. In overweight group, majority had high risk TG and LDL levels and borderline risk HDL levels. Normal TC levels were seen only in 20% of overweight group, remaining had borderline and high risk levels (40%). In obese group, majority had high risk LDL levels, borderline risk TC and HDL levels and normal TG levels. In young age, majority had borderline risk TC and HDL levels and normal TG levels. Normal LDL levels were seen only in 15% in young age, remaining had borderline and high risk levels (42% each). In middle age, majority had borderline risk TC and HDL levels, high risk LDL and normal TG levels. In old age, majority had borderline risk TC and LDL levels but normal TG and HDL levels.

**DISCUSSION**

In this cross sectional study on patients attending comprehensive clinic, the mean lipid levels and prevalence of dyslipidemia were assessed. The study also compared the lipid profile in diabetic and non-diabetic, different BMI categories, different age groups and in males and females.

Mean of lipid parameters in the total population was total cholesterol- 232mg/dl, Triglyceride-172mg/dl, HDL-43mg/dl and LDL- 158.8mg/dl. In other similar studies the mean values were, total cholesterol-197.5mg/dl, Triglycerides-181.7mg/dl, HDL-38.4mg/dl. So our population had different mean lipid values compared to other population.

In our study only 10-11% of population had normal Total cholesterol and LDL levels whereas normal triglyceride and HDL were seen in 44% and 36.6% respectively. Other studies showed the prevalence of normal lipid levels as 46.3% normal LDL, 89.% normal HDL and 45.% had normal TG 5. So the prevalence of dyslipidemia was markedly higher in our population.

The high mean cholesterol levels and higher prevalence of dyslipidemia in our population may be due to genetic factors and lifestyle factors like diet, exercise and urbanization. It is well known that South Asians are at high risk of cardiovascular risk factors including dyslipidemia.

All the four lipid parameters were similar in all age group except for a significantly higher HDL levels, which were more common in old age and middle age compared to young age. Other published studies also showed high incidence of dyslipidemia in middle age and old age.

All lipid parameters were similar in both sexes except for higher TG levels in males. Other studies showed a gradual increase in dyslipidemia in all BMI categories in females. It also showed that percentage of females having dyslipidemia was less as compared to males. Thus our population behaved differently with regards to lipid levels in males and females.

Most of the lipid parameters were similar in all three groups of BMI except for a slightly high Total cholesterol in the obese group and a slightly high triglyceride in the overweight group. Other studies reported prevalence of higher concentration of triglyceride in obese. Here also our study findings was different from published studies.

All lipid profiles were almost similar in diabetic and non-diabetic. Slightly higher mean total cholesterol, triglycerides and LDL were seen in diabetic patients but difference was statistically insignificant. Even the classic diabetic dyslipidemia (high triglyceride and low HDL) were similar in diabetic and non-diabetic. But in other studies the prevalence of dyslipidemia was more in diabetic patient compared to non-diabetic patients. Even when dyslipidemia cut off for LDL was taken as 100, there was no difference between diabetic and non-diabetic. The reason for lack of difference in our study between diabetic and non-diabetic, may be because diabetic patients may be checking their lipid profile earlier and hence being treated earlier. Those who were on treatment were excluded from our study.

Limitations of the study were the relatively small sample size. Multiple logistic regression analysis was not done with different variables of the study.

Thus the distribution and pattern of dyslipidemia in our population were grossly different from literature already reported Larger studies involving more number of patient are required to confirm this study findings.

**CONCLUSION**

This cross sectional study of lipid profile of patients from Kerala shows that the lipid profile profile in our population is different from that in published literature.

**REFERENCES**


Age Influence on Clinical Profile and Outcome of Stroke –
A Hospital based Cohort Study from a Comprehensive Stroke
Care Centre in Kerala, South India

Vivek Nambiar*, Jisha S Das*, Jeslyn Mary Philip*, Delcey Rachel Vargheese*,
Manu Raj***, Remya Sudevan****

ABSTRACT

introduction: Stroke is the most common cause of preventable disability and one of the most common causes of mortality all over the world. Western studies have shown that etiology, risk factors and outcome of stroke in young adults are different from that of older stroke patients. Indian studies regarding the comparison of young and old stroke patients are limited.

objectives: To compare the clinical characteristics, risk factors, etiology, drug utilization patterns, adverse drug reactions and functional outcomes in young and old stroke patients admitted in a comprehensive stroke care centre.

methods: This observational study was conducted in 240 adult patients who were admitted in the Comprehensive stroke care department of a tertiary care hospital for a period of 44 months (January 2012- September 2015). The study duration was three years. Data on type of stroke, risk factors, etiology, type of antithrombotic therapy, recurrence of stroke and adverse drug reactions in patients was collected from medical records and hospital information system using a standard proforma. Follow up on functional outcome, medication compliance and adverse drug reactions to antithrombotic therapy were done by either telephonic interview or direct conversation with the patient or family members. Mann Whitney test was used to compare continuous variables and Chi-Square test was used for categorical variables and p<0.05 was considered significant.

Results: In the present study, 80 young and 160 old patients were studied. Both the groups showed a male preponderance. The commonest type of stroke was ischemic stroke (78.7% young v/s 88.1% old) in both groups. The etiology was undetermined for young patients (40%) while cardiac embolism was the etiology in 32.5% of the old patients. Hypertension was the most common cardiovascular risk factor in both groups (48.7% young v/s 75% old). Aspirin was the most commonly prescribed antiplatelet drug (76.1% young v/s 90% old) in both groups. Both the groups had good compliance to medications and the difference was not statistically significant. Minor bleed was the most common adverse drug reaction (7.5% young v/s 11.2% old) seen. Unfavourable functional outcome was significantly lower in young compared to the old (48% in young patients v/s 72.8%in old patients). Stroke recurrence was seen less in the young compared to old (8.8% v/s 15.1%) patients.

conclusion: There are significant differences in the stroke etiology, risk factors, antithrombotic therapy and functional outcome between the young and old stroke patients.

Key words: Stroke, risk factor, etiology, recurrence

Key Messages: In this era of lifestyle diseases, the prevalence of young stroke has increased. There are substantial differences in the stroke etiology, risk factors, antithrombotic therapy and functional outcome between the young and old stroke patients.

Corresponding Author: Remya Sudevan

INTRODUCTION

Stroke is the most common cause of preventable disability and one of the most common causes of death all over the world. It is an acute focal neurological deficit of vascular origin and includes intracranial haemorrhage, subarachnoid haemorrhage, and cerebral infarct. Age is the most cardinal non modifiable risk factor for stroke. The mean age of acute stroke is 75 years in major epidemiological studies. The incidence rate of total young stroke (< 45 years) ranges from 0.1-0.3 per 1000 person years but most population based epidemiological studies are focused on stroke in the older population. Even though the outcome and etiology of young stroke is unique, comparison studies of young and old stroke patients in India are sparse. In the current study, we compared the clinical characteristics, risk factors, etiologies, drug utilization pattern, adverse drug reaction (ADR) and functional outcome in young and old stroke patients admitted in the Stroke Medicine department of a tertiary care hospital in South India.

SUBJECTS AND METHODS

A single centre observational study was conducted on first ever stroke patients admitted to the stroke department of a tertiary care hospital in South India for a period of 44 months from January 2012 to September 2015. The study period was for three years and was approved by the institutional ethics committee. All patients diagnosed with arterial ischemic stroke, ischemic stroke
RESULTS

During the study period, data from a total of 240 patients with stroke were analysed. Among study subjects, 160 (66.6%) were categorized as old stroke and 80 (33.3%) as young stroke. The mean age of the young stroke population was found to be 38.9 years (21 - 45 years) while in old stroke population, the mean age was found to be 62.9 years (46 - 87 years). Males predominated in both the groups, with 68.8% and 62.5% in the old and young stroke categories, respectively. Ischemic stroke was found to be more common, i.e., 78.7% in young and 88.1% in old group. Thirty three (41.2%) young patients had lesion on the right side while for 79 (49.4%) old patients it was left sided. A major proportion of patients (77.5% young and 75.6% old patients) had cerebral infarcts with higher number of lesions in the anterior region (58.7% in young patients and 56.2% in old patients). A higher percent of young patients had a large lesion compared to the old group (32.5% versus 21.9%).

Cardiac embolism was the etiology for stroke in 52 (32.5%) old patients and 14 (17.5%) young patients and the difference was statistically significant (p=0.0142). The etiology remained undetermined for 32 (40%) young stroke patients. Amyloid angiopathy, lupus vasculitis, antiphospholipid antibody (APLA) syndrome, Moyamoya disease, Takayasu arteritis, and polycythemia attributed to the etiologies in 26.2% of the young population (Figure 1).

STATISTICAL ANALYSIS

The statistical analysis was done by SPSS. Summary values are presented as mean (SD) or percentage (n) as applicable. Mann Whitney test was used to compare continuous variables and Chi-Square test was used for categorical variables. p<0.05 was considered significant.

RESULTS

During the study period, data from a total of 240 patients with stroke were analysed. Among study subjects, 160 (66.6%) were categorized as old stroke and 80 (33.3%) as young stroke. The mean age of the young stroke population was found to be 38.9 years (21 - 45 years) while in old stroke population, the mean age was found to be 62.9 years (46 - 87 years). Males predominated in both the groups, with 68.8% and 62.5% in the old and young stroke categories, respectively. Ischemic stroke was found to be more common, i.e., 78.7% in young and 88.1% in old group. Thirty three (41.2%) young patients had lesion on the right side while for 79 (49.4%) old patients it was left sided. A major proportion of patients (77.5% young and 75.6% old patients) had cerebral infarcts with higher number of lesions in the anterior region (58.7% in young patients and 56.2% in old patients). A higher percent of young patients had a large lesion compared to the old group (32.5% versus 21.9%).

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Among the cardiovascular diseases, hypertension was the most common risk factor in both young (48.7%) and old stroke patients (75%), with a significant difference on comparison (p<0.0001). Table [1] Diabetes mellitus was found to be significantly more in old (63.7%) than young patients (26.3%) and this difference was statistically significant (p<0.0001).

Cardiac valve defects was significantly higher in young patients compared to the old patients (12.5% v/s 3.7%, p=0.0104).

Seventeen young and 29 old patients did not receive any antithrombotic therapy as they had experienced hemorrhagic stroke or ischemic stroke with hemorrhagic transformation or had expired during hospital stay. Aspirin (76.1% in the young and 90% in the old) followed by clopidogrel were the most commonly prescribed antiplatelet agents. Eleven young stroke patients (17.5%) were prescribed anticoagulants compared to old stroke patients (5.3%) at the time of hospital discharge and this difference was statistically significant (p=0.0065).

A total of 180 patients completed 2 years of follow up after first ever stroke. Data was available for 42 young patients (8 patients expired and 5 patients were lost to follow up) and 88 old patients (30 patients expired and 7 patients were lost to follow up). The medication compliance was assessed among these patients under follow up. Among them, 40 (95.2%) young and 78 (88.6%) old patients showed high medication adherence while 1 (2.3%) young patient and 8 (9%) old patients showed low adherence when measured with MMAS.

Adverse drug reactions to antithrombotic therapy were identified in 18 (22.5%) young and 38 (23.7%) old patients with minor bleeds (ecchymotic patches, gum bleed, dysmenorrhoea, and hematuria), gastroesophageal reflux disease and dyspepsia being the most commonly reported ADRs (Figure 2). There was one possible and 17 probable ADRs in the young stroke group while in the older population, out of the 38 ADRs observed, four were categorized as possible and 34 as probable cases.

Length of hospital stay was less than 10 days for majority of both young (57.5%) and old (61.2%) patients. The functional outcome in patients who had completed two years after first ever stroke was unfavourable for 48% of young patients and 72.8% of older patients.

Seven (8.8%) young and 23 (15.1%) old patients experienced recurrence of stroke during the 24 months follow up. The average time to first recurrence of stroke was 6 months in the young and 13 months in the old. Four out of seven young patients and 12 out of 23 old patients succumbed to death due to stroke recurrence.

<table>
<thead>
<tr>
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<th>Young patients n=80</th>
<th>Old patients n=160</th>
<th>p-value</th>
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<td>45(56.3%)</td>
<td>113(70.6%)</td>
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</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>21(26.3%)</td>
<td>102(63.7%)</td>
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</tr>
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<td>Alcoholism</td>
<td>21(26.3%)</td>
<td>40(25%)</td>
<td>0.8339</td>
</tr>
<tr>
<td>Smoking</td>
<td>12(15%)</td>
<td>31(19.3%)</td>
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<tr>
<td>Family History</td>
<td>10(12.5%)</td>
<td>9(5.6%)</td>
<td>0.0629</td>
</tr>
<tr>
<td>Migraine</td>
<td>10(12.5%)</td>
<td>6(3.7%)</td>
<td>0.0140</td>
</tr>
<tr>
<td>Obstructive Sleep Apnoea</td>
<td>1(1.3%)</td>
<td>3(1.9%)</td>
<td>0.7214</td>
</tr>
</tbody>
</table>

Table 1: Risk factors
DISCUSSION

Stroke subtypes, etiology and risk factors

The mean age of stroke in the old population was found to be lower than that in the western population. Our study shows that the male patients are predominant in both the young and old category which is consistent with other studies. This can be attributed to early accumulation of traditional risk factors in men than in women as well as socio-cultural differences in India where more strokes in males reaches to the tertiary care centers. Ischemic stroke accounts for about 85% of all strokes worldwide and the current results are also in agreement. Hemorrhagic stroke was slightly more prevalent in the young patients probably due to uncontrolled hypertension owing to delayed diagnosis.

The results showed no difference in the laterality of lesion which is in contrast to a hospital based study in North India which showed majority of patients with left sided lesion. There was no significant difference in the brain region affected between the two groups.

Etiology of stroke was classified according to TOAST criteria. Large artery disease was found to be more prevalent in elderly due to atherosclerotic disease. In our series, we detected 17.5% young patients with large artery disease which is slightly less compared to previous reports. Significantly higher frequency of cardio embolic stroke seen in the elderly could be due to the referral bias as ours being a tertiary care centre where most of the critically ill patients are referred. These patients had multiple issues like cardiac failure and concurrent severe coronary artery disease.

Rate of small vessel disease was lesser than that reported in other studies as most of the minor lacunar strokes are managed in the local hospitals rather than a tertiary care hospital like ours. The uncommon causes of stroke were significantly more in younger than in older population. It must be due to the significant number of young hemorrhagic patients than old supported by several studies indicating that hemorrhagic stroke accounts for more than 50% of all stroke under the age of 45 years.

Regarding the localization of brain infarct; in the young, more than half of the patients had anterior infarct akin to other studies. There was no significant difference in posterior infarct among the two groups in contrast to the Helsinki stroke registry study that found considerably higher posterior infarct in age below 45 years. The probable reason is the high prevalence of dissections as a cause of stroke in young people in the developed countries as they are more active physically and involved in contact sports.

Studies have shown that although modifiable risk factors are same in young and old population, the prevalence differs between the two groups. In our study, the older population showed significantly higher frequency of cardiovascular risk factors (like hypertension, dyslipidemia and myocardial infarction) and diabetes mellitus compared to the young population which is in agreement with other stroke risk factor studies. Migraine and valvular heart disease were more frequently seen in younger population similar to other studies.

The risk of future strokes can be reduced by controlling these modifiable risk factors. There was no significant difference in rates of stroke recurrence between the two groups. The recurrence rate of stroke in young patients seen in our study was comparable to another with recurrence rate of 11.1%.

Antithrombotic therapy, adherence and adverse events

Anticoagulants were found to be prescribed more in
the young than the old even though cardio embolic stroke was highly prevalent in the old population. This may be attributed to the good tolerability and good health status of the young population. Anticoagulants are also prescribed in case of stroke due to thrombo-philic disorders (protein C, protein S deficiency, APLA syndrome) which was more prevalent in the young.

Both groups showed good compliance to antithrombotic therapy. Low compliance was observed more in the old population which may be due to the presence of various co morbidities resulting in polypharmacy.

Adverse drug reactions due to antithrombotic therapy were found in both young and old population without considerable difference. Bleeds were more common in the old probably due to the presence of concurrent co morbidities. The functional outcome after a 24 month follow up showed a more favourable outcome in the young patients compared to the old patients which is in accordance with studies elsewhere18.

CONCLUSION

There are significant differences in the stroke etiology, risk factors, functional outcome and anticoagulant therapy between the young stroke patients and patients in the older population. More multi-center studies including registries will help to advance the knowledge of young stroke and its preventive and therapeutic strategies.

REFERENCES

4. Smajlovic D. Strokes in young adults: epidemiology and preven-
5. Weimar C, Diener HC. Antiplatelet therapy and oral anticoagu-
7. Putaala J, Metso AJ, Metso TM, Konkola N, Kraemer Y, Haapa-
niemi E, Kaste M, Tatistumak T. Analysis of 1008 consecutive pa-
10. Adams HP Jr, Butler MJ, Biller J, Toffol GJ. Non hemorrhagic cere-
12. SiqueiraNeto JI, Santos AC, Fabio SR, Sakamoto AC. Cerebral in-
16. James E, AnnieJ, Nambiar V. Impact of clinical pharmacist’s inter-
A Case of Non Bacterial Thrombotic Endocarditis in Elderly

Aswin Rajeev*, George Paul*, Priya Vijayakumar*

ABSTRACT

Non bacterial thrombotic endocarditis is a rare entity and usually a post mortem diagnosis. Some patients present with features of embolism ante-mortem. We are presenting a case of non bacterial thrombotic endocarditis which was detected incidentally in a patient with squamous cell carcinoma of the oesophagus.

Corresponding Author: George Paul

INTRODUCTION

Nonbacterial thrombotic endocarditis (NBTE) is a rare condition that refers to a spectrum of non infectious lesions of the heart valves that is most commonly seen in advanced malignancy. NBTE is often an autopsy finding. However, some patients are diagnosed ante-mortem presenting with the signs and/or symptoms of systemic embolization and require therapy.

Initiating factor for pathogenesis of NBTE is not known but endothelial injury in the setting of a hypercoagulable state is thought to be critical for development of NBTE. Endothelial damage by circulating cytokines like tumour necrosis factor and interleukin 1 may trigger platelet deposition particularly in the presence of activated coagulation system in conditions like malignancy, disseminated intravascular coagulation and anti-phospholipid syndrome to result in local deposition of platelets and molecules.

Compared to vegetations in infective endocarditis, vegetations of NBTE are easily dislodged since there is little inflammatory reaction at the site of attachment. Thus in NBTE, there is a greater tendency for vegetation to embolize and cause extensive infarction.

Patients with nonbacterial thrombotic endocarditis (NBTE) are typically asymptomatic until embolization occurs. The investigation should focus on evaluating the patient for the signs and symptoms of embolization, obtaining an echocardiogram, and defining the underlying cause. There are no laboratory tests that confirm the diagnosis of NBTE. Hence testing is directed in distinguishing NBTE from infective endocarditis.

A high index of clinical suspicion is critical for the diagnosis of NBTE. Despite therapy the prognosis from NBTE is generally poor

CASE REPORT

A 68 year old male who is a known case of squamous cell carcinoma mid oesophagus with metastasis s/p chemo-radiotherapy one year ago presented with complaints of breathlessness even at rest since one month. He also had fatigue, reduced appetite and was bed bound. There was no history of fever, chest pain or any other constitutional symptoms. On examination he was found to have tachycardia, enlarged supraclavicular lymph nodes and a peri-umbilical mass. Respiratory system examination showed generalized reduced vesicular breath sounds with no added sounds. His blood investigations showed leucocytosis with elevated inflammatory markers and thrombocytopenia. Blood culture was reported to be sterile. CT chest and abdomen showed enlarged supraclavicular and para-aortic nodes with multiple metastatic lesions in both lung fields. An Echocardiogram was done in view of tachycardia which showed two friable masses in right ventricle one of which was attached to anterior tricuspid leaflet and other to right ventricular apex. A diagnosis of non bacterial thrombotic endocarditis was considered. Patient was started on low molecular weight heparin and was discharged with plan to continue with palliative approach. The patient expired after 2 months of discharge.

DISCUSSION

Patients with malignancy have a hypercoagulable state, and NBTE is a condition whereby there is valvular deposition of fibrin and platelets. Patients often present with signs and symptoms of systemic embolization from the vegetations. The vegetations are particularly prone to embolization, as they have little inflammatory reaction at the site of attachment with little cellular organization. Cardiac murmurs are infrequent. In a patient with underlying malignancy and echocardiogram detected vegetation, persistent fever in the presence of serial negative blood cultures coupled with lack of response to antimicrobial therapy should increase suspicion of NBTE.

Nonbacterial thrombotic endocarditis (NBTE) is a rare condition most often found post-mortem with rates in autopsy series ranging from 0.9 to 1.6 percent. It has been reported in every age group, most commonly affecting patients between the fourth and eighth decades of life with no sex predilection. Patients with advanced malignancy and those with systemic lupus erythematosus are the most common populations affected by NBTE.

One autopsy series reported that, compared to the general population, patients with underlying malig-
nancy have a higher rate of NBTE (1.25 versus 0.2 percent)\textsuperscript{2,3}. When compared to other malignancies, higher rates were reported in those with adenocarcinoma (eg, lung, colon, ovary, biliary and prostate) (2.7 versus 0.47 percent) with the highest rates observed in patients with mucin-secreting and pancreatic adenocarcinoma (10 percent) \textsuperscript{4}.

NBTE should be suspected in patients with acute stroke or coronary ischemia with underlying cancer, systemic lupus erythematosus, or anti phospholipid syndrome. It should also be suspected in patients with acute stroke or multiple widely distributed emboli of unknown aetiology as well as in those with presumed infective endocarditis who are unresponsive to, or progressing poorly on, antibiotic therapy \textsuperscript{5,6}.

**Key Points**

- Non bacterial thrombotic endocarditis is a rare entity and usually a post mortem diagnosis.
- Some patients present with features of embolism ante-mortem.
- A high index of clinical suspicion is critical for the diagnosis of NBTE. Despite therapy the prognosis from NBTE is generally poor.

**REFERENCES**

Phenytoin Toxicity in an Adolescent with Epilepsy Following Self Harm – Is Early Detection of Depression Imperative?

Kotchuthressia Mathew*, Kesavankutty Nayar*, Sreekumar*, Dinesh Narayanan*

ABSTRACT
Depression is often unrecognised and untreated, leading to higher chance of suicidal ideation in adolescents with epilepsy. We describe a case of an adolescent, a known case of myoclonic seizure disorder presented with symptoms of phenytoin toxicity following alleged history of consumption of phenytoin tablets. This report emphasises the necessity in early diagnosis and treatment of depression in the patients with epilepsy.

Key Words: Phenytoin toxicity, Adolescent, Epilepsy, Depression

INTRODUCTION
Depression is highly common in adolescents with epilepsy. The prevalence of depression is estimated to be 23-26%1,2. Unfortunately it is often unrecognised and untreated, leading to higher chance of suicidal ideation in such adolescents. The following case presents phenytoin toxicity in a patient with myoclonic seizures who consumed his father’s regular antiepileptic medicines (phenytoin). The case is to demonstrate the features of phenytoin toxicity in the patient. We also highlight the necessity of treating depression in the patients with epilepsy.

CASE REPORT
Mr A, 17 year old single male studying in 11th standard, a known case of myoclonic seizures was maintaining well on Sodium Divalproate 200 mg for one year. He had family history of generalised seizure disorder in father who was on phenytoin. In June 2016, he presented to the emergency department with one episode of vomiting and difficulty in walking with swaying to one side (with no history of fall, bucking or tipping episode). On CNS examination, there was bilateral gaze evoked nystagmus. His cerebellar signs were positive. He had bilateral dysdiakinesia and finger nose test was positive bilaterally. Heal knee test was positive gait was ataxic and planters were bilaterally flexors. Blood was sent for toxicology. The serum toxicology results were positive for phenytoin. His phenytoin level was 41.8 mcg/ml (Therapeutic range 20-40 mcg/ml). Urgent gastric lavage was given and he was treated with activated charcoal. EEG was taken which was normal. On mental status examination, there was bilateral gaze evoked nystagmus. His cerebellar signs were positive. He had bilateral dysdiakinesia and finger nose test was positive bilaterally. Heal knee test was positive gait was ataxic and planters were bilaterally flexors. Blood was sent for toxicology. The serum toxicology results were positive for phenytoin. His phenytoin level was 41.8 mcg/ml (Therapeutic range 20-40 mcg/ml). Urgent gastric lavage was given and he was treated with activated charcoal. EEG was taken which was normal. On detailed history taking, he admitted of consuming his father’s regular antiepileptic medicines, phenytoin tablets. On mental status examination, he admitted of consuming his father’s regular antiepileptic medicines, phenytoin tablets. On mental status examination, Ideas of helplessness, hopelessness, worthlessness and suicidal ideations were present. He was started on Escitalopram 20 mg for his low mood and suicidal ideation. After three days of admission, Sodium Divalproate 600 mg was restarted by the neurology department for controlling myoclonic seizures. Psychotherapy sessions were done. Patient improved symptomatically at the time of discharge. He was maintained on Sodium Divalproate 600 mg for his seizure disorder and Escitalopram 20 mg for depressive disorder. On follow up, his affect improved and suicidal ideations were absent.

DISCUSSION
This patient with myoclonic seizures who had underlying depressive disorder presented to us with unsteady gait and bilateral nystagmus. This prompted us to suspect deliberate self harm by the subject and sent blood for toxicology. Eventually serum toxicology was positive for Phenytoin. Most common presenting features of phenytoin toxicity happen to be unsteady gait, vertigo, vomiting, drowsiness & generalised weakness. Toxic effects are manifested as nystagmus, loss of smooth pursuit, cerebellar defects, and eventually, coma.

One of the most common psychiatric comorbid conditions in patients with epilepsy is depression. The etiology or the risk factors for depression in children and adolescents with epilepsy are likely multifactorial, involving neurobiological, psychosocial, and iatrogenic risk factors. Depression in children with epilepsy poses considerable challenges, such as higher suicide risk and a more severe course. Suicidal ideation and attempts are more likely to be seen in children and adolescents with epilepsy than in the general pediatric population3,4.

Depressive symptoms can present according to the temporal relation to the seizures occurrence into ictal, perictal (symptoms precede and/or follow the seizure occurrence), and interictal (symptoms occur independently of the seizure occurrence). Interictal depression is the most frequently “recognized” type of mood disorder and can present differently among patients.

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with epilepsy. A significant proportion of patients with epilepsy and depression are not diagnosed nor offered the appropriate treatment.

Kanner et al determined that 63% of epileptic patients with depression remained symptomatic for one year before treatment was initiated. It is necessary to screen epileptic patients for depression. The depression scales such as Hospital Anxiety and Depression Scales, Becks Depression Inventory or Neurological Disorder Depression Inventory (NDDI-E) can be used.

For the treatment of depression in adolescents with epilepsy, pharmacotherapy accompanied by cognitive-behavioral approaches in selected children seems to be the most efficacious means of management. SSRIs such as sertraline and fluoxetine were good therapeutic options in terms of remission of depression symptoms and number of side effects. The SSRIs that seem less likely to inhibit CYP450, and therefore have the least potential for interaction with other drugs, including AEDs, are citalopram, escitalopram, and sertraline.

Adverse effects of AED monotherapy or polytherapy in addition to antidepressant medications can complicate the clinical picture and should be taken into account. The risk of seizures is significantly higher with TCAs in comparison with SSRIs and hence TCAs are not recommended. Bupropion, has been shown to lower seizure threshold in a dose-dependent manner. The case report emphasises the need of early diagnosis and treatment of underlying depression in patients with epilepsy. Early diagnosis and effective treatment decreases the duration of depression, increase the patients compliance with Anti Epileptic Drug and improves the Quality Of Life.

REFERENCES
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