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Twenty Years (1996-2015) Trend in Suicide by Hanging in the Transkei Sub-region of South Africa

Banwari L Meel

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Abstract

Background: In the Xhosa culture, suicide by hanging is viewed very negatively. However, recently hanging has been on the increase in the Transkei sub-region of South Africa. Poverty, unemployment, alcoholism and HIV may play a role in these deaths.

Objective: To study 20 years' (1996-2015) trend in suicide byhanging in the Transkei sub-region of South Africa (1996-2015).

Method: This is a retrospective descriptive study from the records of Mthatha Forensic Pathology Laboratory.

Results: Over a period of 20 years (1996-2015), 24 693 medico-legal autopsies were performed in the Transkei sub-region of South Africa. Of these, 1 555 (6.3%) deaths were recorded as being the result of hanging. The average rate of hanging is 17.3 per 100 000of the population per year. The majority (88.5%) were males. The rate of hanging has increased from 8.3 per 100 000 in 1996 to 16.7 per 100 000 of the population in 2015. The male-to-female ratio is 1:7.7 (1376/179). The highest number of hangings, 484 (5.5/100 000),was recorded among males between 21 and 30 years, while among females of 11 to 20 years, 66 (0.75/100 00) such deaths occurred over a period of 20 years.

Conclusion: The incidence of suicide by hanging has doubled in the Transkei sub-region of South Africa over a period of 20 years. It is more common among young adult males. This health crisis needs urgent attention.

Keywords: Suicide; Hanging; Self-harm; Death.

Introduction

Suicide is the second leading cause of death in the 15-25 year age group1and is the 15th leading cause of death worldwide.[1]An estimated 800 000 deaths by suicide occur worldwide every year. According to the WHO, approximately 1.53 million people will die annually from suicide by 2020 worldwide. Although the prevalence of suicide in "low and middle-income countries (LAMIC)" is lower than in high-income countries (11.2 vs. 12.7 per 100 000 people), 75.5% of deaths by suicide occur in LAMIC countries[1].Eight of the ten countries with the highest prevalence of suicide in the world are LAMICcountries.1The WHO (1999) reported that in 1990 suicide accounted for about 8% of non-natural deaths worldwide.[2]

No reliable statistics are available nationally on the suicide rate in South Africa. The only source of epidemiological mortality data is the National Injury Mortality Surveillance System (NIMSS), which is not complete as data were not taken from rural settings.[3] The national annual number of deaths resulting from injury was estimated at 68 930 in 2000,[4]although indications are that this figure has been decreasing since 1996.[5] The NIMSS figures for 2003 showed that suicide accounted for 11% of all non-natural deaths in South Africa.[6] South Africa ranked eighth internationally for its high suicide rate, but no statistics are available in support of the argument.[7] The South African

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Federation of Mental Health (SAFMH) has also disputed the ranking, as has the World Health Organisation. The SAFMH does not accept this ranking, but offers no alternative ranking or even an indication of whether the suicide rate is high or low in South Africa.

An earlier study carried out by the author in the same region, Transkei, showed that there was an increasing trend of hanging that increased from 5.2 per 100 000 (1993) to 16.2 per 100 000 over a period of ten years (1993-2003)[8]. The highest incidence was in the 20-to-29-year age group[8]. Financial hardship was the main underlying cause, identified in 87% of cases of suicide.[9] The economic recession has increased the rate of suicide and unemployment worldwide[10].

A study carried out in pregnant women in rural South Africa has shown that there is increase in HIV prevalence rate from 35.3% to 39% in between 2001 and 2013[11]. HIV/AIDS has a significant association with suicide[12]. The author strongly suggested that breaking the vicious cycle of unemployment, alcohol abuse and poor health, along with comprehensive poverty, through poverty alleviation programmes could be an important step in reducing suicides in the Transkei sub-region of South Africa[9] and indeed in other at-risk areas globally.

The aim of this study is to determine the trend of suicide by hanging in the Transkei region of South Africa, and related causative factors or triggers of suicide.

Method

This is a retrospective descriptive study from 1996 to 2015 on all unnatural deaths in the Transkei sub-region of South Africa. The former Transkei has five functioning mortuaries, situated in different local municipalities; the one serving Mount Fletcher is in Elundini, that serving Mount Frère in Mzimvubu, the one serving Bizana in Mbizana, that for Lusikiski in Ingquza and Mthatha mortuary serves four local municipalities and a district municipality.

Data were collected on a data sheet with columns for the post mortem number, date, age and gender of the deceased, as well as the cause of death. These data were transferred by a research assistant to an Excel program and then analysed. The result was displayed in the form of tables and figures. The study received ethics clearance from the Ethics Committee of University of Transkei (now it is Walter Sisulu University).

Results

Between 1996 and 2015 (20 years), 24693 forensic autopsies were carried out on deceased who had died non-natural deaths (Table 1). Of these, 1555 (6.3%) deaths were recorded as suicide by hanging. Hanging ranks in the fifth position -1376 (7.08%) -among males as a cause of unnatural death, and 10thposition-179 (3.34%) -among females in the Transkei sub-region of South Africa (Table 1).

Table 1: Rank and percentage of cause of unnatural deaths by gender in Umtata area.

Rank	Males (n=19,361)		Females (n=5,332)		Total (n=24,693)	
	Cause of death	(n) %	Cause of death	(n) %	Cause of death	(n) %
1	Stabbing	(4376) 22.5	MVA	(1631) 30.45	MVA	(5896) 23.77
2	MVA	(4265) 21.93	Gunshot	(650) 12.13	Stabbing	(4830) 19.47
3	Gunshot	(2921) 15.02	Poisoning	(530) 9.89	Gunshot	(3571) 14.40
4	Assault	(2255) 11.60	Stabbing	(454) 8.47	Assault	(2667) 10.75
5	Hanging	(1376) 7.08	Assault	(412) 7.69	Hanging	(1555) 6.27
6	Drowning	(934) 4.80	Drowning	(325) 6.07	Drowning	(1259) 5.08
7	Collapse	(1519) 7.81	Collapse	(529) 9.87	Collapse	(2048) 8.26
8	Poisoning	(609) 3.13	Burns	(266) 4.97	Poisoning	(1130) 4.59
9	Burns	(423) 2.18	Lightening	(192) 3.58	Burns	(689) 2.78
10	Fall	(357) 1.84	Hanging	(179) 3.34	Fall	(492) 1.98
11	Lightning	(273) 1.40	Fall from height	(135) 2.52	Lightening	(465) 1.87
12	Suffocation	(53) 0.27	Gas suffocation	(29) 0.54	suffocation	(82) 0.33

Table 2: Incidence of hanging in the Transkei sub-region of South Africa (1996-2015).

Year	Estimated population	Females N=179	Rate/100 000 (Females)	Males N=1376	Rate/100 000 (Males)	Total (n=1555)	Rate per 100 000
1996	350 000	6	1.7	23	6.6	29	8.3
1997	358 050	7	2.0	24	6.7	30	8.7
1998	366 285	7	1.9	41	11.2	48	13.1
1999	374 710	8	2.1	40	10.7	48	12.8
2000	383 328	8	2.1	37	9.7	45	11.7
2001	392 145	8	2.1	44	11.3	52	13.4
2002	401 164	4	1.0	47	11.7	51	12.7
2003	410 391	12	2.9	44	10.7	56	13.6
2004	419 830	8	1.9	48	11.4	56	13.3
2005	429 486	1	0.2	64	14.9	65	15.1
2006	439 364	14	3.2	75	17.2	89	20.4
2007	449 469	13	2.9	107	23.9	120	26.8
2008	459 806	9	2.0	98	21.3	107	23.3
2009	470 381	11	2.3	94	20.0	105	22.3
2010	481 199	8	1.7	110	22.9	118	24.5
2011	492 266	8	1.6	82	16.7	90	18.3
2012	503 588	12	2.4	107	21.2	119	23.6
2013	515 170	15	2.9	108	21.0	123	23.9
2014	527 018	8	1.5	105	19.9	113	21.4
2015	539 139	12	2.2	78	14.5	90	16.7
Average	438 140	7.5	2.1	37.5	15.2	77.7	17.3

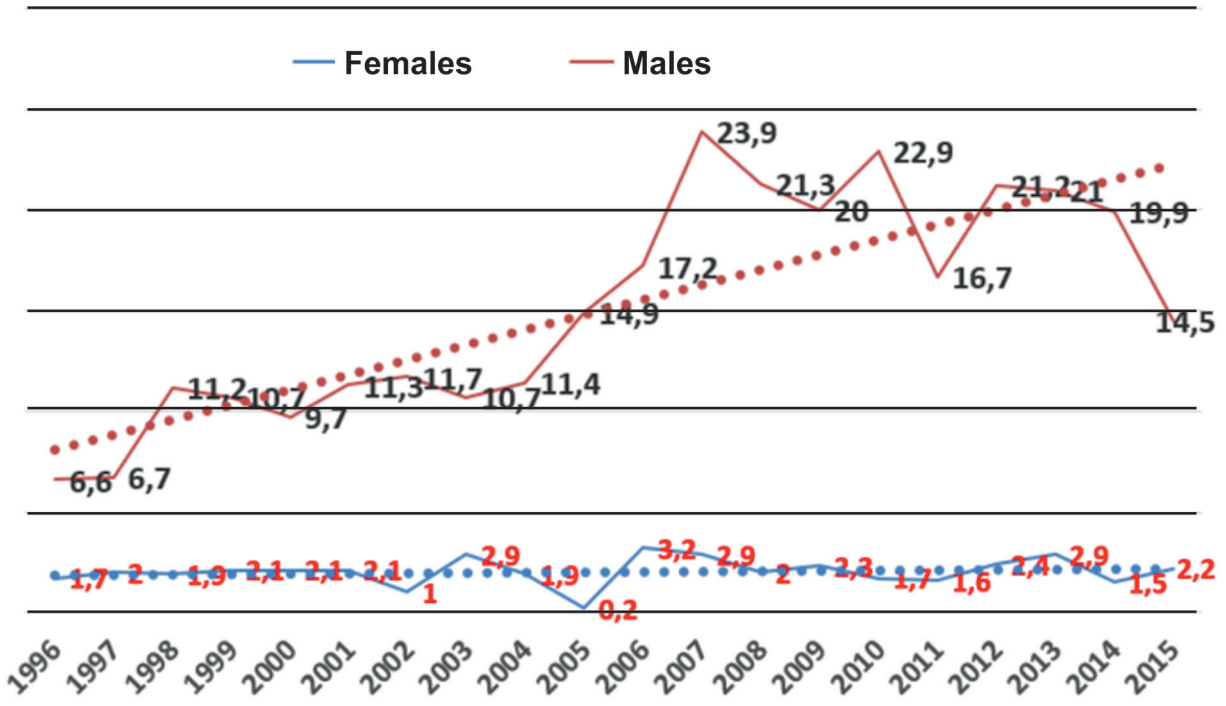

Fig. 1: Rate of hanging among both genders in Transkei sub-region of South Africa (1996-2015) (n=1555).

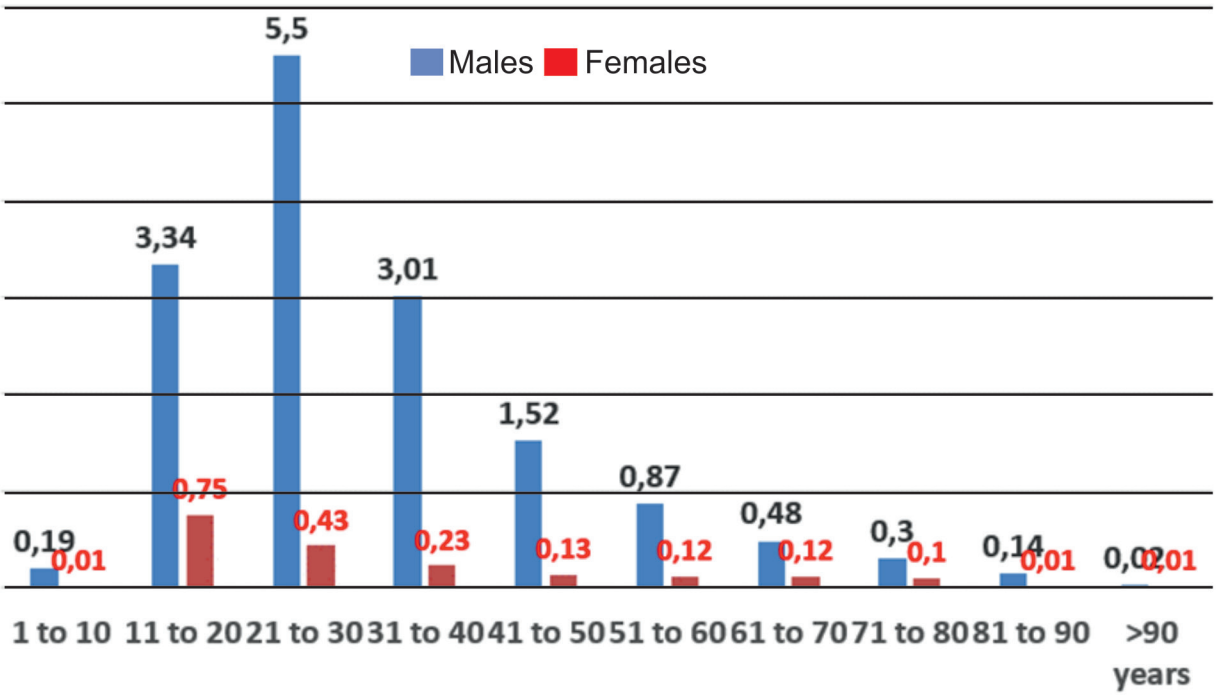

Fig. 2 Rate of hanging per 100 000 of population per year in different age groups in both genders in Transkei sub-region of South Africa (1996-2015) (n=1524).

The average number of hangings was 17.3 per 100 000 over a period of 20 years (1996-2015) of the population per year in this region (Table 2). The majority (88.5%) were males (Table 2). The rate of hanging increased from 8.3 per 100 000 of the population in 1996 to 16.7 per 100 000 in 2015 (Table 2). The highest rate of hanging was 26.8 per 100 000 in 2007 and the lowest was recorded at 8.3/100 000 in 1996 (Table 2). There was a sharp increase in hanging from 10.7 per 100 000 (2003) to 23.9 per 100 000 (2007) among males (Table 2). It decreased after that date to 14.5 per 100 000 among males in 2015 (Table 2).Among females, the incidence of hanging is almost constant but at a lower level (Figure 1). The rate of female hanging was 1.7 per 100 000 in1996 and increased to its highest level of 3.2/100 000 in2006 (Table 2). The female-to-male ratio is 1:7.7 (1376/179) (Table 2). The highest number of hangings was recorded as 484 (5.5/100 000) among males aged between 21 and 30 years, while among 11-to-20-year-old females it was 66 (0.75/100 000) in this study over a period of 20 years (Figure 2).

Discussion

Former Transkei isa low socio-economic rural area of South Africa, with a high rate of unemployment and poverty.[13] It is a disadvantaged region as few job opportunities are available as it is rural without any business activities in the area.[13] The unemployment rate is very high because of the high illiteracy rate and this has led to a high number of permanently unemployed people in this region.[13] Poverty is severe in the Transkei region and it is a partly a legacy of apartheid.[13] Seventy-three percent of the people living in the rural Eastern Cape were living on less than R300 per month in 2005/2006, and more than half them on less than R220 per month [13].

This study, spanning 20 years (1996-2015), revealed that hanging alone accounted for 1 555 (6.27%) non-natural deaths (Table 1). Hanging is the number one cause of death after homicide and accidents in this study (Table 1).It is difficult to assess that how many people committed suicide by other methods, such as shooting, self-poisoning, jumping from height, burn and railway tract injuries. Since there is stigma attached to suicide, there is a tendency to shy away from the truth. The truth is often not disclosed because of the difficulty of having claims paid by insurance companies.[14] Self-harm mortality is high in South Africa despite of the fact that all efforts were used to reduce the mortality.[15] There is no report available on poisoning deaths by the state laboratories in South Africa and specimens were remained unanalysed for years because of heavy backlog.[16] The National Injury Mortality Surveillance System (NIMSS) report showed that poisoning is not among the top

10 external causes of death in South Africa[3],however it has occurred in the Transkei sub-region of South Africa and is ranked the eight most common cause of non-natural deaths (Table 1). The local Xhosa tribe that inhibits this area believes in the use of traditional medicines to cure their illnesses.[17]

The average rate of hanging was 17.3 per 100 000 per year in this study (Table 2). The prevalence of suicide by hanging alone is one and a half times (17.3 vs. 11.2) higher in this sub-region of Transkei than in LAMIC, and a little less than one and a half times (17.3 vs. 12.7) the rate in in middle-income countries[1]. Nertshiombo et al reported in 2012 that in South Africa hanging accounted for 36.2% of non-natural deaths, followed by shooting (35%) and then by other methods (28.8%), such as poisoning, gassing and burning.[18]

It means that the overall rate of death by suicide is around 34.6 per 100 000 of the population of the Transkei sub-region per year (lower estimate), assuming the proportion of hanging, poisoning and shooting as 33% each.[19] It means the overall suicide rate in this region is at least twice higher than the international rate of suicide (the international average is 16 per 100 000 per year).[16] An earlier study published in an American journal by the author mentioned 16.2 per 100 000 of the population in 2003[8], while this study indicates the rate as 13.6 per 100 000 of the population in the same year (Table 2). This discrepancy in the rate is because of the annual increase in the population (3%) was taken into account in this study (Table 2). In this study, the population was assumed to be 410391, which is more realistic than the number used in the earlier study, and this brought down the rate of hanging from 16.2 to 13.6 per 100 000 of the population (Table 2). The denominator was consistent with a population300 000 in the earlier study published in 2003.[8] Further verification is the fact that the total number of suicides in this study was 56 in 2003, and if one should use the same denominator of 2003, i.e. 300 000, then the calculation yields the same result, 13.6/100 000 (56/300 000=13.6), in this study as well (Table 2).

Deaths as a result of firearm injuries decreased by more than half, from 27/100 000 in 1993 to 12.8/100 000 in 2015, in Transkei region of South Africa.[20] This happened after the Firearm Control Act was passed in 2002 by the South African parliament.[21] It is not clearby which percentage suicide by firearm has decreased in this region of South Africa. Too little data on suicide in rural parts of South Africa is available to make comparison with this study possible. A retrospective study on mortuary data carried out in Durban in KwaZulu-Natal indicated that the number of suicides had increased from 14.53 (2006) to 15.53 (2007) per 100 000.[22] Suicide is considered a problem of metropolitan areas, but this is not true, as the Transkei is a vastly rural area of South Africa.[22] The prevalence rates for suicidal behaviour based on apartheid-era data are considered under-representative, since research among the majority black population living in rural areas of South Africa was largely neglected.[23] The hanging rate almost doubled from 8.3 per 100 000 in 1996 to 16.7 per 100 000 in 2015 (Table 2 and Figure 1). Figures released for South Africa in the last decade have shown that hanging and shooting were the preferred methods for committing suicide, followed by self-poisoning with agents such as pesticides and overdoses of substances.[2] The number of hangings was lowest (8.7 per 100 000) in 1997 and highest (26.8 per 100 000) in 2007(Table 2 and Fig.1).

There were great expectations from the government after liberation in 1994, but it did not keep promises such as low-cost housing and employment.[13] A sharp increase in hanging occurred from 2005 (15.1 per 100 000) to 2007 (26.8 per 100 000) (Table 2 and Figure 1). Although there is no proof of why people commit suicide, financial difficulties were observed in 87% of cases as an underlying cause in the Transkei region of South Africa.[9] The Transkei is characterised by worsening poverty, where the average rural income was R255 per month in 2005/06, well below the poverty line drawn by the South African government.[13]

Hanging is a method of choice predominantly among males (Table 2 and |Figure 2). The male/female ratio in this study is 7:1 (Table 2 and Figure 2), which is more than double the international ratio of 3:1.[24] China is the exception, where the rate of female suicide is consistently higher than that of men, particularly in rural areas.[24] Malesconsequently often succumb to financial difficulties, lack of self-esteem, unemployment and excessive alcoholism, resorting to self-harm as a result.[25] Transkei is known for supplying mineworkers to South Africa. Most of the people who were formerly employed worked in mines and they resigned or were retrenched at a young age, returning to the Transkei region in a poor state of health (78.2%).[26] They knew that they would not find employment again.[25] In Xhosa culture, a man is the provider of food for his family, but once he is unemployed, he is forced to depend on his spouse, causing loss of pride that is culturally unacceptable.[25]

Alcohol consumption rates in South Africa are the highest in the world and continue to rise.[27] Research demonstrates that the population consumes in excess of 5 billion litres of alcohol annually.[28] A study conducted by Matzopolous in 2005 showed that there was considerable variation in the distribution of alcohol-related injuries in South Africa.[29] The rate of hanging varied less among females (1.7 per 100 000 in 1996 to 2.2 per 100 000 in2015) than among their male counterparts (Table 2 and Fig. 3).The highest rate of hanging (5.5/100 000) was recorded among males between 21 and 30 years in this study (Table 3 and Fig. 2).

This is similar to the rate mentioned in an earlier report by the author (2009), which showed that more than half (55%) of the hangings involved people younger than 30 years.Less than one quarter (23%) of these victims were younger than 20 years.[30] This is in contrast to statistics from developed countries, where suicide rates were, by and large, higher in older age groups[31]. It is difficult to explain the reason for young adults committing suicide by hanging. HIV infection and psychiatric disorders have a complex relationship. HIV infection could lead to psychiatric disorders, and psychiatric patients are more vulnerable to HIV infection.[32] About 300 million people in the world are suffering from depression, which is the leading cause of suicide[33].

Conclusion

There is an increasing trend in suicide by hanging in the Transkei sub-region of South Africa. The incidence of hanging has doubled in this region over a period of 20 years. About two-thirds of suicide victims are young, from 11 to 30 years. An in-depth study is required to determine the risk factors associated with hanging in this region of Transkei in South Africa.

Ethical Issues

The author has ethical permission for collecting data and publication (approved project No. 4114/1999) from the Ethical Committee of the University of Transkei, South Africa.

Conflict of interest

The facts in this report could be submitted in demand. The references were not labelled but can be produced if necessary.

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Original Article

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Traumatic Spinal Cord Injuries in South Costal Region of Andhra Pradesh

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Abstract

Background: Traumatic Spinal Cord Injury (TSCI) is serious health problem among adults. It leads to significant morbidity, mortality, permanent disability and socio-economic effect. The present study was conducted in Narayana Medical College, Nellore State Andhra Pradesh.

Aims and Objectives: To know the common age group that is mostly prone to TSCI, sex

difference of TSCI,the area of distribution of TSCI cases, mode of injury, various management modalities like Surgical, ICU stay etc and their role in the prognosis of patients with TSCI,the site of injury commonly involved and GCS of patients admitted due to TSC.To know the mortality rate among TSCI patients.

Type of study: This is a two years retrospective and oneyear prospective study.

Place of study:Spinal cord injuries admitted in Narayana Medical College & Hospital – Nellore, during the years 1st October 2010 to 30th September 2013.

Material and Methods: All patients admitted and managed for traumatic spinal cord injury were retrieved and data collected in a pre-designed proforma. Patient characteristics, details of etiology, mechanism of injury, level of injury, extent of neurological deficits, details of investigations, details of management and immediate outcome were recorded.

Observations and Discussion: The maximum cases 40 were in the age group of 41-50(26.31%). The mean age is 38.45 + 14.56.SCI cases were more common among males 115(75.66%), than in females 37(24.34%) and also the most common age group was between 41- 50 years 33(21.71%) followed by 21-30 years 30(19.73%). Male to female ratio was 4.18: 1.It was observed that maximum cases were in rural area 132(86.80%), followed by urban area 20(13.20%). It was observed that most common cause was fall from height 93(61.20%), followed by road traffic accidents 52(34.20%). It was observed that most common site of injury was cervical 67(44.10%), followed by lumbar 54(35.50%), thoracic 29(19.10%), thoracolumbar 2(1.30%).

Conclusion: Traumatic spinal cord injuries affect young population and can leave these persons with significant functional and physical morbidity. Male persons are more commonly injured than females.

Key words: Spinal cord injury; Spinal injuries; Spinal trauma.

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Introduction

The cervical spine,beingthe most mobile portion of the spine,is the most common site of spinal injuries. An estimated 12000-14000 spinal cord injuries occur each year out of the total of 200000 traumatic spinal column injuries in the United Staes.[1-6] Nearly 10000 patients will die each year as a result of an injury to the spinal cord.[5,7-10] The most frequent age group to suffer an injury to the spinal cord is 15-30 years,motor vehicle accidents, falls, and sports being the most common mechanisms

of injury[2,5,11-13]. The cause of spinal injury varies with age, and particularly sex, with males being three to four times as likely to sustain an injury than females. Age is also a determinant of the type of spinal injury as children less than 4 years of age have fewer vertebral injuries than adults[14]. The injuries in young pediatric population tend to occur between the occiput and C2, representing 40% of all pediatric spine injuries, whereas only 20% of adult spinal injuries occur at this level. [1,14-16]Anatomical differences of the pediatric spine includes ligaments laxity, incompletely ossified and wedge-shaped vertebral bodies, shallow and horizontal facet joints, and underdeveloped neck muscles.[14,15] Subluxation injuries without fracture and spinal cord injuries without radiographic abnormality(SCIWORA) are very rare in adults and occur sometimes in young persons.[14,15,17]

Neurological Injury

Up to 15% of patients sustaining spinal injury secondary to trauma show a neurological injury as a result.[5, 13] Injuries to the cervical spine, in particular, result in a much higher incidence of injury to the spinal cord than at any other spinal level. The incidence of spinal cord injury ranges from 2% to nearly 100% of cervical spine injuries, depending on the cervical level involved, with an incidence of 40%-60% overall.[1,2,5,7-11,18,19] The incidence of spinal cord injury with cervical fracture is likely to be underestimated as some patients may die prior to medical attention. This is particularly true for atlanto-occipital dislocation, where 25% of patients may die as a result of respiratory arrest prior to evaluation.[4,5,13]

In 2003 the worldwide incidence of spinal cord injury ranged from 9.2 to 50 persons per 1 million populations. Technological advances and improved medical care have increased both the physical survival and functional capabilities of persons with disabilities to a level that would have been unthinkable even a few years ago. The prevalence of Spinal Cord Injury worldwide is estimated to be around 500 per million populations. From the available literature, it is known that majority of the individuals will be in the age group of 20-30 years with a male preponderance (M: F ratio: 3-4:1). Traffic related injuries were the primary cause for 50-60% of Spinal Cord Injuries, followed by falls (20- 30%), Sports and occupational injuries (5-10%). About 70% new cases of Spinal Cord Injury appear in less than 30 years of age. A review of literature from around the world reveals that the incidence of Traumatic spinal cord injury varies from 9- 53 per million per year.[20]

One of the comprehensive study undertaken by the Shanta Memorial Rehabilitation centre at Bhubhaneshwar in Orissa, the annual incidence of spinal cord injuries was 20 per million population per year for the period 1985- 1990. The male to female ratio was 3: 2. Nearly 50% of Spinal Cord Injury subjects were in between 20-40 years. Falls, Road traffic accident, and fall of objects were the major underlying causes in 53%, 26% & 12% respectively.[20]

A careful epidemiological study and trends of traumatic spinal cord injuries can provide information regarding magnitude of the problem of spinal trauma and resultant demand on medical and social resources; and can help identify the risk factors involved and actual causes of spinal cord injury.

So, this study is taken up to help in formulating preventive measures which may modify or eliminate the risk factors and may decrease the incidence of spinal cord injuries.

Aims and Objectives

As stated earlier TSCI is serious condition resulting in loss of human life or survivor disability or issues related to sexuality and sexual functions resulting in family and social disharmony.

Advances in medical field in the management, investigative procedures, and patient care have drastically decreased the mortality and morbidity in TSCI.

To understand the magnitude, pattern, factors and other demographic profile of TSCI comprehensive studies are essential.

With this view in mind this study was carried out involving the 3 years data (two years retrospective and one year prospective) of 152 patients admitted to Narayana Medical College and Nellore from 1st October 2010 to 30th September 2013 with TSCI. The data is analysed with a view to achieve the following aims.

1. To know the common age group that is mostly prone to TSCI.
2. To know sex difference of TSCI.
3. To know the area of distribution of TSCI cases.
4. To know the mode of injury.
5. To know various management modalities like Surgical, ICU stay etc andtheir role in the prognosis of patients with TSCI.
6. To know the site of injury commonly involved and GCS of patients admitted due to TSCI.
7. To know the mortality rate among TSCI patients.

Materials and Methods

Source of Data

This is a two years retrospective and one year prospective study carried out involving 152 cases of

spinal cord injuries admitted in Narayana Medical College & Hospital – Nellore, during the years 1st October 2010 to30th September 2013.

Inclusion Criteria

- All cases of spinal cord injuries admitted during the years 1st October 2010 to 30th September 2013.
- These cases include both direct admissions as well as referral cases.
- Suicidal and Accidental cases of spinal cord injuries are included.

Exclusive Criteria

- Cases of homicidal spinal cord injuries were not included, as no such case was reported during the study years.
- This study is a hospital based study and hence Postmortem findings were not considered.

Materials

Case sheets pertaining to this study were obtained from Medical Records Section with permission from the competent authorities.The case sheets thus obtained were studied for the following details.

Patient Characteristics

1. Name
2. Age/Gender
3. IP.NO
4. Occupation
5. Contact Information and Contact Number
6. Locality

Pre-Hospital Details

1. Cause of Injury
2. Date of Injury
3. Time of Injury
4. Mechanism of Injury
5. Pre-Hospital Care

ER Care

1. Neurological Status At Er Arrival
2. Level Of Injury
3. Blood Pressure
4. Respiration
5. Respiratory Rate
6. Pulse
7. SPO2
8. Intubation
9. GCS
10. Fluid Management
11. X-Rays
12. MRI
13. CT Scan Brain

Management

1. Icu Care
2. Ventilation
3. Chest Care
4. Medical Management (Conservative)
5. Surgical Management
6. Duration of Hospital Stay

Outcome

1. Neurologically Improved
2. Remained The Same
3. Died

Follow Up Complications

All these details were documented in a proforma and are analyzed by Using Microsoft Excel – 2007

This study has the approval of Institutional Ethics Committee. (IEC)

Observations and Results

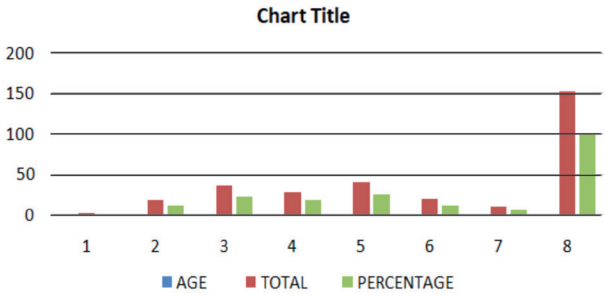
This study is a two years retrospective and one year prospective study carried out involving 152 cases of spinal cord injuries admitted in Narayana Medical College & Hospital – Nellore, during the years 1st October 2010 to30th September 2013.Details of the patient like name, age, gender, IP No, occupation, contact information and contact number , locality, cause of injury, date of injury, time of injury, mechanism of injury, pre-hospital care, neurological status, level of injury, blood pressure, respiration,respiratory rate,pulse,Spo2,intubation, GCS,fluid management, X-rays, MRI, CT scan brain, ICUcare, ventilation, chest care, medical management (conservative),surgical management, duration of hospital stay and outcome are noted. The above details are statistically analyzed.

Table 1: Table No. 1 and Bar Diagram 1 shows Age wise distribution of SCI admitted in Narayana Medical College, Hospital between 1st October 2010 to 30th September 2013.

Age Wise Distribution		
Age	Total	Percentage
0-10	2	1.31
11-20	18	11.84
21-30	35	23.02
31-40	28	18.42
41-50	40	26.31
51-60	19	12.50
> 61	10	6.57
	152	100

Table No.1 reveals the maximum cases 40 were in

Bar Diagram - 1



the age group of 41-50(26.31%), followed by 21-30(23.02%) and least number of cases were in the age group of less than 10 years (1.31%) followed by more than 61 years(6.57%). The mean age was 38.45 + 14.56.

Table No. 1 and Bar Diagram 1 shows Age wise distribution of SCI admitted in Narayana Medical College, Hospital between 1st October 2010 to 30th September 2013.

Table 2: Table no. 2 and Bar Diagram 2 shows Sex wise distribution of SCI .

Sex Wise Distribution in Various Age Groups						
Age Distribution	Male	%	Female	%	Total	%
0-10	0	0	2	1.31	2	1.31
11-20	15	9.86	3	1.97	18	11.84
21-30	30	19.73	5	3.28	35	23.02
31-40	16	10.52	12	7.89	28	18.42
41-50	33	21.71	7	4.60	40	26.31
51-60	13	8.55	6	3.94	19	12.50
> 61	8	5.26	2	1.31	10	6.57
Total	115	75.66	37	24.34	152	100

Bar Diagram - 2

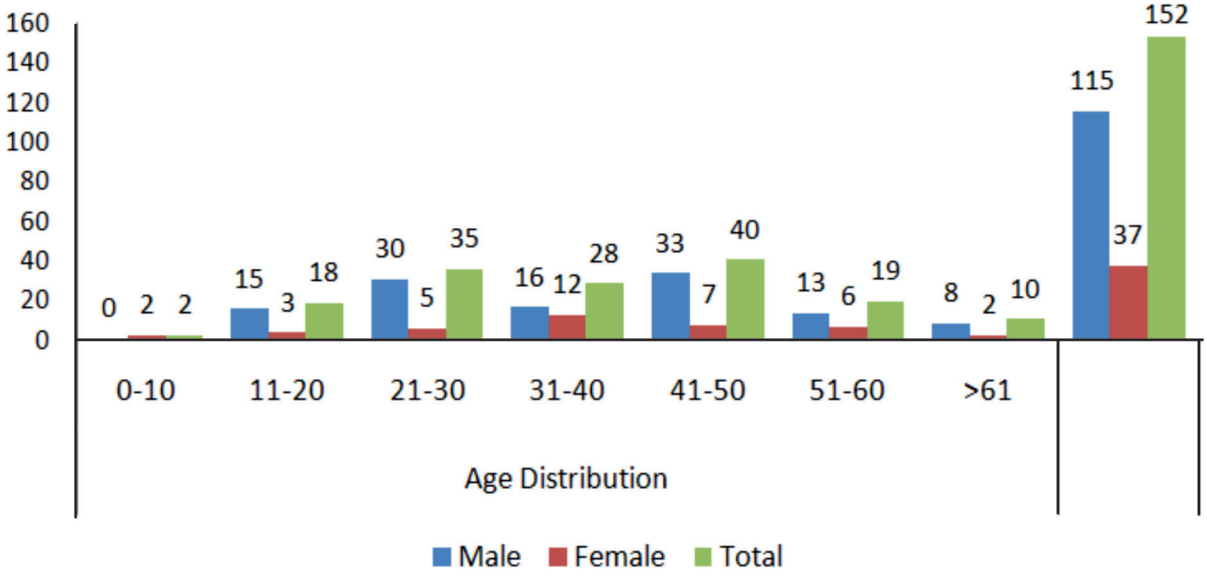


Table No. 2 reveals SCI cases were more common among males 115(75.66%), than in females 37(24.34%) and also that in males the age group involved was between 41- 50 years(21.71%) followed by 21-30 years(19.73%).Where as in females the common age group involved between 31-40 years followed by 41-50 years. The least age group involved in males was 0-10 i.e. no cases found, in females 0-10 years (1.31%) and more than 61 years (1.31%). Male to female ratio was 4.18: 1

Table 3: Table No. 3 and Bar Diagram 3 shows Area wise distribution of SCI cases.

Area Wise Distributon		
Area	**Frequency**	**Percentage**
Rural	132	86.8
Urban	20	13.2
Total	152	100

Bar Diagram - 3

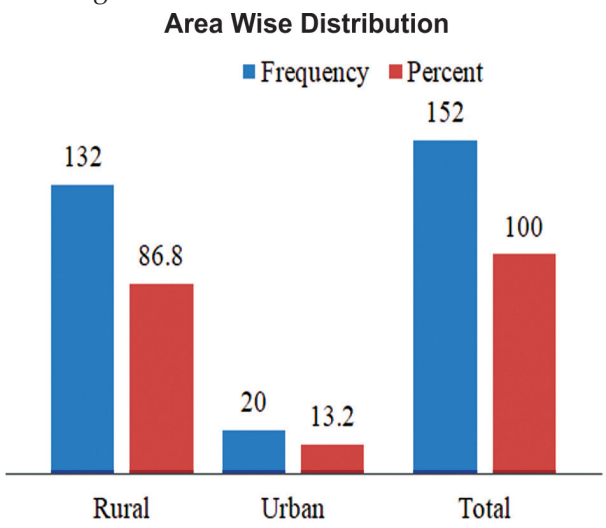


Table no.3 reveals that maximum cases noted in

rural area 132(86.80%), followed by urban area 20(13.20%).

Table 4: Table no. 4 and Bar Diagram 4 shows Mode of injury.

Mode of Injury		
Mode	Frequency	Percentage
MVA	52	34.2
Fall From Height	93	61.2
Other Causes	7	4.6
Total	152	100

Bar Diagram - 4

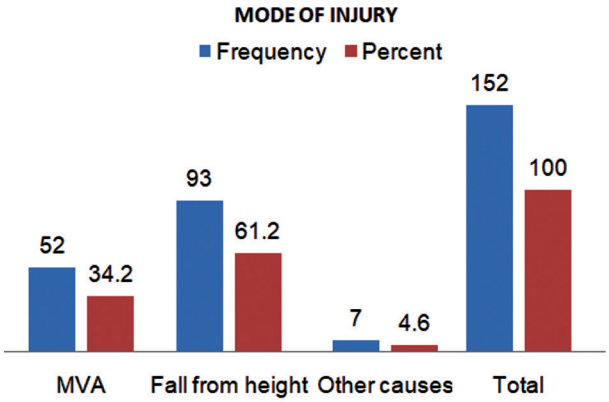


Table no.4 reveals that most common cause was fall from height 93(61.20%), followed by MVA 52(34.20%).

Table 5: Reveals that most common site of injury was cervical 67(44.10%), followed by lumbar 54(35.50%), thoracic 29(19.10%), thoracolumbar 2(1.30%).

Level of Injury		
Level	**Frequency**	**Percentage**
Cervical	67	44.1
Thoracic	29	19.1
Thoracolumbar	2	1.3
Lumbar	54	35.5
Total	152	100

Bar Diagram - 5

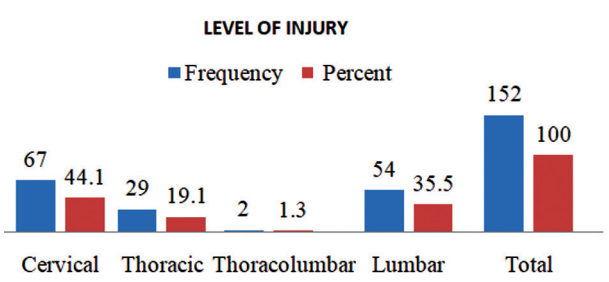


Table no. 5 reveals that most common site of injury was cervical 67(44.10%), followed by lumbar 54(35.50%), thoracic 29(19.10%), thoracolumbar 2(1.30%).

Table 6: Table no.6 and Bar Diagram 6 shows CT scan brain requirement.

CT Scan Brain		
	Frequency	**Percentage**
Yes	26	17.1
No	126	82.9
Total	152	100

Bar Diagram - 6

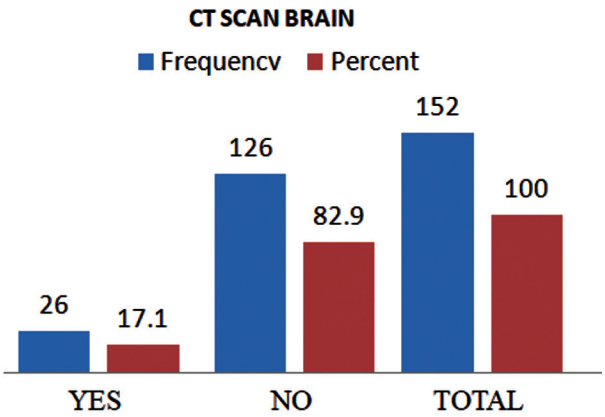


Table no. 6 reveals the 26(17.10%) patients required CT scan brain to rule out brain injury.

Table 7: Table no. 7 and Bar Diagram 7 shows ICU stay requirement.

ICU Stay		
ICU Stay Required	**Frequency**	**Percentage**
Yes	64	42.1
No	88	57.9
Total	152	100

Bar Diagram-7

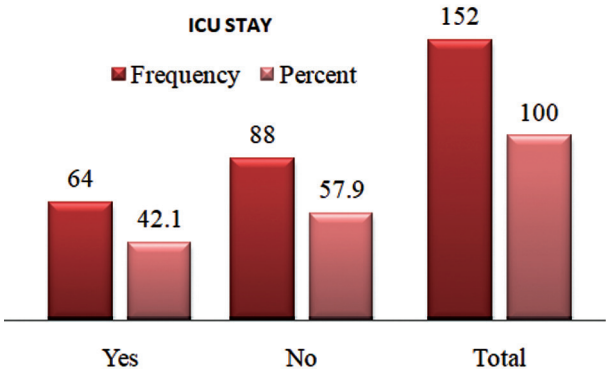


Table No. 7 reveals the 64(42.10%) patients

required ICU stay indicating that they had more complications.

Table 8: Table no. 8 and Bar Diagram 8 shows surgical management.

Surgical Management		
	Frequency	Percentage
Spinal Fusion	118	77.6
Laminectomy	12	7.9
Conservative	22	14.5
Total	152	100

Bar Diagram - 8

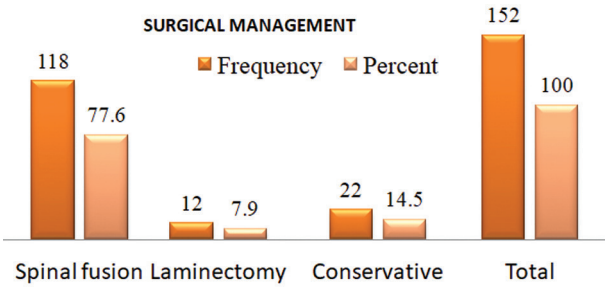


Table no. 8 reveals that 130 patients (85.52%) required surgical management out of 118 patients (77.60%) spinal fusion, 12 patients (7.90%) laminectomy and 22 patients(14.50%) managed conservatively.

Table 9: Table No. 9 and Bar Diagram 9 shows Prognosis and Mortality.

Prognosis and Mortality		
Prognosis	Frequency	Percentage
Alive	141	92.8
Dead	5	3.3
Referral	6	3.9
Total	152	100

Bar Diagram-9

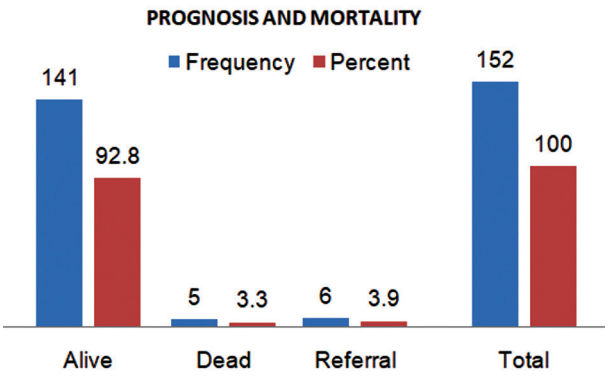


Table no. 9 reveals 5 cases (3.30%) died and 147 cases (96.71%) were alive. However of which 6 cases (3.90%) were referred and went to othercentersand their prognosis is not known.

Table 10: Table no.10 and Bar Diagram 10 shows GCS.

GCS		
Score	Frequency	Percentage
3	3	1.94
4	3	1.94
10	3	1.94
11	3	1.94
12	12	7.90
13	3	1.94
14	10	6.6
15	115	75.7
Total	152	100

Bar Diagram - 10

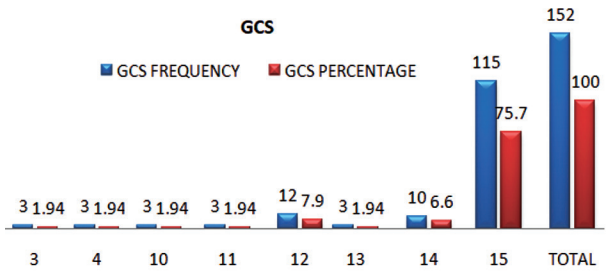


Table no. 10 reveals GCS score 15 was seen in 115 patients (75.70%), score 12 in 12 patients (7.90%) and score 14 in 10 patients (6.60%) indicating good prognosis and remaining patients with comparatively bad prognosis.

Discussion

This is a two years retrospective and one year prospective study carried out involving 152 cases of spinal cord injuries admitted in Narayana Medical College & Hospital – Nellore, during the years 1stOctober 2010 to 30th September 2013 and the following observations were noted.The maximum cases 40 were inthe age group of 41-50(26.31%), followed by 21-30(23.02%) and least number of cases were in the age group of less than 10 years (1.31%) followed by more than 61 years (6.57%). The mean age is 38.45 + 14.56.SCI cases were more common among males 115(75.66%), than in females 37(24.34%) and also the most common age group was between 41- 50 years 33(21.71%) followed by 21-30 years 30(19.73%).

In females the common age group involved was between 31-40 years was 12(7.89%) followed by 41-50 years was 7(4.60%). 0-10 age group in males showed no case, in females2 cases(1.31%) and in more than 61 age group 2 cases(1.31%).Male to female ratio was 4.18: 1.It was observed that maximum cases were in rural area 132(86.80%),

followed by urban area 20(13.20%).It was observed that most common cause was fall from height 93(61.20%), followed by road traffic accidents 52(34.20%).

It was observed that most common site of injury was cervical 67(44.10%), followed by lumbar 54(35.50%), thoracic 29(19.10%), thoracolumbar 2(1.30%).It was observed that 26(17.10%) patients required CT scan brain to rule out brain injury.It was observed that 64(42.10%) patients required ICU stay indicating that they had more complications.It was observed that 130 patients (85.52%) required surgical management out of 118 patients (77.60%) spinal fusion, 12 patients (7.90%) laminectomy and 22 patients (14.50%) managed conservatively. It was observed that 5 patients (3.30%) died and 147 patients (96.71%) were alive. However of which 6 patients (3.90%) were referred and went to other centers and their prognosis is not known. It was observed that GCS score 15 is seen in 115 patients(75.70%), score 12 in 12 patients(7.90%) and score 14 in 10 patients(6.60%) indicates good prognosis and remaining patients had bad prognosis.

Comparitive Analysis

This is a two years retrospective and one year prospective study carried out involving 152 cases of spinal cord injuries admitted in Narayana Medical College and Hospital – Nellore, during the period from 1stOctober 2010–30th September 2013. Details of the patient like name, age, gender, IPNo, occupation, contact information and contact number, locality, cause of injury, date of injury, time of injury, mechanism of injury, pre-hospital care, neurological status, level of injury, blood pressure, respiration ,respiratory rate,pulse,spo_2,intubation, GCS, fluid management, X-rays, MRI, CT scan brain, ICU care, ventilation, chest care, medical management (conservative),surgical management duration of hospital stay and outcome are noted. The above details are statistically analyzed.

Age wise distribution of SCI reveals more common age group is 41-50 were 40(26.31%) and 21-30 were 35(23.02%) followed by 31-40 were 28(18.42%), 51-60 were 19(12.50%), 11-20 were 18(11.84%), 61+ were 10(6.57%), 0-10 were 2(1.31%). A study done by, Hong-Yong Feng[31], show that largest group was 45-54 years followed by 35-44 years. A study done by, Roop Singh[23] shows that most prevalent age group was 20-29 were 203(42.03%), followed by 30-39 were 128(26.50%).

A study conducted by, Ziniya Mustarya Rahman[25] shows the most prevalent age group was 25-32 were 114(26.76%), followed by 43-75 were 106(24.88%). A study conducted by, Suraj Bajracharya[27] shows that most prevalent age group was 21-41 were 350(39.10%). A study conducted by, Asrvatham Alwin Robert[28] shows higher frequency in the 21-30(40.00%) and 31-40(19.70%) age groups. A study conducted by, Marleem Schonherr[29] shows higher frequency in age groups is 21-40 and 61-70 years. A study conducted by, F. Biering – Sorensen [30] shows higher frequency in age group is 15-24 years including 40% of all cases.

A study conducted by, Ravi Shankar. B G.[20] shows most prevalent age group was 31-40 were 16(40.00%), followed by 18-30 were 14(35.00%). A study conducted by, A. Soopramanien[26] shows that most prevalent age group was 51-60 were 88(21.40%) followed by 31-40 were 68(16.50%).

Sex wise distribution reveals SCI is more common in males 115(75.66%) than females 37(24.34%). Male to female's ratio is 4.18: 1. In the studies conducted by, Ravi Shankar. B G[20,] Roop Singh[23,]Liis Sabre [24,]ZiniyaMustary Rahman[25],A. Soopramanien[26,] Suraj Bajracharya[27,] MarleemSchonherr[29,]F. Biering –Sorensen[30,]Hong – Yong Feng[31,]Donna M. Dryden [32,] C Lan[33,]Guang – Zhi Ning[34] shows similar findings i.e. male dominance is noted. Area wise distribution of SCI reveals rural population 132 (86.80%) is more than urban population 20(13.20%). In the studies conducted by, ZiniyaMustary Rahman[25,] Donna M. Dryden[32] shows similar findings that SCI was more common in the rural than urban area.Mode of injury in SCI reveals fall from height 93 (61.20%) is more common than Motor Vehicle Accident. In the studies conducted by Roop Singh [23,] Ziniya Mustarya Rahman[25], A. Soopramanien[26],Suraj Bajracharya[27], Hong- Yong Feng [31] also shows similar findings that SCI was more common in Fall from height followed by Motor Vehicle Accidents.However studies conducted by,Liis Sabre, [24]Asirvatham Alwin Robert,[28]F. Biering – Schonherr[30,] Donna M. Dryden,[32]C Lan [33,] Guang – Zhi Ning [34] shows that Motor Vehicle Accident was more common than Fall from height.Level of injury in SCI reveals cervical spine fracture 67(44.10%) is more common followed by lumbar 54(35.50%), Thoracic 29(19.10%) and Thoracolumbar 2(1.30%).

In the studies conducted by Liis Sabre [24,] Ziniya Mustary Rahman [25,] Suraj Bajracharya,[27]Asirvatham Alwin Robert,[28] MarleemSchoherr,[29] F. Biering – Schonherr,[30]Hong –Yong Feng[,31] and Donna M. Dryden[32] also showed that SCI was more common at cervical level. However study conducted byRoop Singh[23] reveals that Dorsolumbar spine

injury was the commonest fractured vertebra.ICU Stay in SCI reveals 64(42.10%) patients required and 88(57.90%) patients not required. A study conducted by Steven Casha[35]shows that 66% of patients that required ventilation did so within 48 h and that 19% required greater that 8 weeks of ventilationSurgical Management in SCI reveals spinal fusion 118(77.60%) followed by conservative treatment 22(14.50%), laminectomy 12(7.90%). In a study conducted by, A. Soopramanien[26] shows that bone grafting (38.20%), laminectomy (6.90%), plates and screws (3.70%).

The study conducted by,Suraj Bajracharya[27] shows 216 (93%) out of 233 patients were treated conservatively, compared to operative treatment in 17(7.00%) patients in the initial five years of the study period. Prognosis and mortality reveals 141 (92.80%) patients alive, 5(3.30%) patients dead and 6(3.90%) was referral to other others centers. A study conducted by, Liis Sabre [24]shows all patients with SCI, 162(27.22%) of whom were dead. A study conducted, A. Soopramanien[26] shows the mortality rate in the early days post injury fell from 22% (retrospective studies) to 10.1% (prospective studies). A study conducted by, Hong- Yong Feng [31] shows 8 patients died after operation.

Summary and Conclusions

The maximum cases were in the age group of 41-50(26.31%), followed by (23.02%).The least number of cases were in the age group of less than 10 years (1.31%) followed by more than 61 years (6.57%). The mean age is 38.45 $\pm$ 14.56.SCI cases are more common among males 115(75.66%), than in females 37(24.34%).In males the most common age group involved is between 41- 50 years (21.71%) followed by 21-30 years(19.73%). In females the most common age group involved was between 31-40 years followed by 41-50 years. The least age group involved in males was 0-10 i.e. no cases found, In females the least age group involved was 0-10(1.31%) and more than 61(1.31%). Male to female ratio is 4.18: 1.It was observed that maximum cases noted in rural area 132(86.80%), followed by urban area 20(13.20%).It was observed that most common cause was fall from height 93(61.20%), followed by Road traffic accidents 52(34.20%).It was observed that most common site of injury is cervical 67(44.10%), followed by lumbar 54(35.50%), thoracic 29(19.10%), thoracolumbar 2(1.30%). It was observed that 26(17.10%) patients required CT scan brain to rule out brain injury.It was observed that 64(42.10%) patients required ICU stay indicating that they had more complications.It was observed that 130 patients (85.52%) required surgical management.Out of 130 patients 118 (77.60%) underwent spinal fusion, 12(7.90%) underwent laminectomy and 22 patients(14.50%) were managed conservatively.It was observed that 5 patients (3.30%) died. 147 cases (96.71%) were alive. However 6 cases (3.90%) were referred and went to other centers and their prognosis was not known. It was observed that GCS score 15 is seen in 115 patients(75.70%), score 12 in 12 patients(7.90%) and score 14 in 10 patients(6.60%) indicates good prognosis and remaining patients had bad prognosis.

Limitations and Recommondations

Though the studies was conducted in tertiary centre due to location and availability of established centre within reach. The study population is limited. The sample size is small.Post mortem findings not including because post mortem conducted in other hospital. No information was available about referral case. SCI are most commonly associated with fall, road traffic accidents and sports.The above activities commonly involve active age groups ranging from 20-50 years, this age group commonly involved in SCI. TSCI results in socio – economic and domestic issue as it involve age group of 20-50 years and also males who are in the prime financial support of the family and also sexually active age.

One of the commonest causes of SCI is falls which are occupation related in young age group and in older age group due to age related instability. This can be prevented by taking necessary safety precautions in both work places, public places and in houses placing signs like slippery surface, rails for support and making necessary adjustment in house especially in bath rooms of elderly and aged. Road traffic accidents contribute to TSCI (railway spine, whiplash injury).

This can be avoided by making mandatory provisions for seat belts, head rest in all seats in cars and vehicles. Strict traffic rules to avoid accidents and patrolling to check drunk drivers. Sports activities contribute to TSCI (Probably caused Brazil to lose the world cup because of spinal injury to Neymar, a football player). This is on raise due to increased speed in sports. This can be avoided by passing stringent rules, usage of proper measures, educating the players about prevention etc. As this study is limited to a smaller area, smaller group and short duration, we recommend studies in larger area, larger group and longer duration.

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Original Article

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Cross Sectional Study of Severe and Mixed Malaria Infections : Experience of a Tertiary Care Hospital in South-West Coastal Karnataka

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Abstract

Background: India launched the National Framework for Malaria Elimination to encourage surveillance and strategies towards 'elimination' rather than control by 2030. Considering the significant challenges on this path, regional variations in clinical and haematological manifestations are useful parameters to help shape national elimination strategies. Our study aims to compare the demographic, clinical and haematological parameters among severe malaria cases and highlight mixed malaria infection.

Methods: A cross sectional study was carried out between January 2015 and May 2018. Diagnosis was done by peripheral smear microscopy, followed by immunochromatographicrapid test and finally quantitative buffy coat test. Patients were classified as severe and non-severe disease according to WHO major criteria. The relevant data of the study subjects was collected from inpatient case records and analysed.

Results: A total of 403 inpatients with confirmed malaria were included in our study. Severe malaria was observed in 21.5% and these patients had a significantly longer stay in hospital of 6.08 ± 3.78 days. Infections caused by P. falciparum (48.6%) and P. vivax (46.9%) were almost equal in number. Acute respiratory distress syndrome was observed more in 21.4% (9/42) of P. vivax infections. Mixed malarial infections were observed in 4.5% (18/403) of total patients and 33% of mixed malarial cases presented with severe manifestations.

Conclusions: Attributing severe malaria to P. falciparum or P. vivax alone can be misleading especially in regions with complicated epidemiology, like India. Identification of malarial coinfectionsinfection are difficult without molecular diagnostic tools. Incorrect diagnosis may directly affect appropriate antimalarial therapy selection.

Highlights

- Clinical and haematological manifestations have not been observed as a malaria burden metric in all regions.
- Identification of malarial coinfectionsinfection are difficult without molecular diagnostic tools.
- Appropriate laboratory diagnosis of mixed malarial infections aids in selecting antimalarial therapy.
- Study of regional variations in malaria presentations can improve public health.

Keywords: Malaria co-infection; Plasmodium; India; Endemic; Eradication.

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Background

Malaria remains a significant global health problem with 228 million cases worldwide in 2018[1]. India accounts for 4% of the globally reported cases and reports 70% of total malarial cases in south east Asia due to the endemicity of plasmodium parasites to this region[2]. Global co-operative efforts to reduce the malaria burden have allowed hyperendemic regions such as India to report a 24% decrease

since 2016[3]. This reduction in cases is credited to the national malaria control program (NMCP) and the national vector borne disease control program (NVBDCP) launched by the government of India. However, despite significant national efforts, malaria continues to make up one of the common inpatient diagnoses in India.

Malaria is highly endemic and persistent throughout the year in several parts of southwestern regions of India, including a substantial portion of Karnataka state. Of the 27 districts, Udupiharbours high vector density contributing to the high case incidences (0.1-1 confirmed cases per 1000 population) in this region.[1] The NVBDCP identified Udupi as the second highest district reporting 1028 cases of malaria from April 2016 to March 2017[4]. Considering the high endemicity and huge health burden, additional reports maybe required on demographic, clinical and hematological factors that contribute to severe malaria manifestations in coastal tropical regions like Udupi. As malaria is a dynamic disease that disproportionately affects the rural poor, its epidemiology is affected by construction, poverty, and changing global climate; making continual investigation necessary [5]. Therefore, in line with global malaria eradication goals by 2030, it is useful to assess potential changes in the distribution, presentation and severity of malaria to prepare for future malaria-specific interventions[5–8]. The present study aims to compare the demographic details, clinical features, haematological parameters, complications among severe malaria; as well as highlight mixed malaria infection.

Methodology

2.1 Study design &population :A retrospective cross sectional timebound study was conducted following approval by Institutional Ethics Committee, IEC No.–672/2019. Demographic, clinical and laboratory data from inpatients with laboratory diagnosis of malaria for 3.5 years, between January 2015 and June 2018 admitted for > 48 hours was collected in pre-designed detailed case record forms. Outpatients being treated for malaria were excluded from study. On the basis of clinical presentation, inpatients were then classified as severe and non-severe malaria according to WHO major criteria and further analysed.

2.2 Study definitions : Criteria for classification of plasmodium infection as severe malaria is defined by WHO; including dangerous manifestations like thrombocytopenia, pulmonary edema, respiratory distress syndrome and impaired consciousness (See additional file 1).[9,10] Patients with coinfection with P. falciparum and P. vivax were laboratory confirmed cases by microscopy and rapid diagnostic test.

2.3 Malaria diagnostics :Diagnosis of patients included in the study was performed on peripheral blood samples by conventional microscopy, followed by rapid diagnostic test (immunochromatographic method) and finally quantitative buffy coat (QBC) test during the study period as per standard guidelines.

2.5 Peripheral smear : Thin smears were examined according to WHO recommendations.[1] Thin smears were made to identify malaria species (including the diagnosis of mixed infections), quantify parasitaemia, and assess for the presence of schizonts, gametocytes. Negative result have been reported after screening at least 200 OI visual fields under 1000x magnification. The level of parasitaemia may be expressed either as a percentage of parasitized erythrocytes or as the number of parasites per microliter of blood, however was not recorded in present study.

2.6 Rapid diagnostic test :MalariaP.f/P.v antigen (SD BIOLINE, Abott, California, USA) was used to detect circulating parasite antigens targeting histidine-rich protein-2 (HRP-II) for P. falciparum and lactate dehydrogenase for P. vivax (pLDH). The test was performed using 5µl of anticoagulated venous blood; the sample was added to specimen well and 4 drops of assay diluent was added to square well. The test was interpreted as per the manufacturer's instructions after 15 min. It was recorded as positive for P. falciparum or P. vivax if P.f and P.v bands respectively were seen, along with control (C) band.[11]

2.7 Quantitative buffy coat test : QBC technique (Kapillery, FlorotekBiosystems, Mumbai, India) was used for the detection of malarial parasites in blood using microhematocrit tubes coated with acridine orange 65µl of blood and stopper and float were added at either ends into the tubes. The tubes were centrifuged at 12000rpm in a pre-programmed centrifuge as per the kit instructions. The visualisation was done using a fluorescent microscope under 100x objective. Parasites were found to have bright green fluorescence at the interface between RBC and buffy coat layer.

Mixed malarial infections were identified as a combination of mixed morphology (P. falciparum and P. vivax) microscopy and rapid diagnostic test with positive P.f along with P.v bands.

2.8 Malaria Management: Patients confirmed to have malaria were treated according to national

recommended guidelines i.e., chloroquine (25mg/kg) for 3 days along with primaquine (0.25mg/kg) for 14 days for vivax malaria. Falciparum malaria treatment was either chloroquine for 3 days along with single dose primaquine on the second day or artesunate–sulfadoxine–pyrimethamine combination therapy (fixed dose of artemisin combination therapy, ACT) for 3 days along with single dose of primaquine on the second day.[3] Any patients admitted for malaria management was based on treating clinician discretion.

2.9 Statistical Analysis: The relevant demographic, clinical and laboratory data of the study subjects was recorded and evaluated with SPSS ver. 16 (SPSS Inc., Chicago, IL, USA). Quantitative data was presented as mean ± SD or median, IQR. Chi-square test was used to test significance between categorical variables. Independent sample t test was used to compare means across two groups. The level of significance for all statistical tests was set at 5% ($p < 0.05$) and the results were reported within 95% confidence interval.

During study period, a total of 403 patients were included in the study and the majority, 340 (84.4%) were male. Almost all patients were clinically stable on discharge, only 1 patient was discharged against medical advice. P. falciparum infection was reported in 196 (48.6%) of the patients and P. vivax infection was found in 189 (46.9%) patients as illustrated in table 1. Severe malarial infections showed a significantly longer stay in hospital at a mean 6.08 ± 3.78 [p <0.001, OR 0.783 (95% CI 0.703 – 0.873)].

3.2 Characteristics of severe malarial infection caused by P. falciparum and P. vivax.

Severe malaria, classified according to WHO (2014) has been reported in 87 (21.5%) cases.[9] Mixed malaria cases were excluded and were analysed separately. Furthermore, majority of severe infections were due to P. vivax(42/82, 51.8%). Clinical and laboratory criteria have been tabulated in table 2. Interestingly, previous history of malaria was significantly associated with P. falciparum [p = 0.010, OR 2.273 (95% CI 1.76 – 2.93)].

Clinical presentations of severe infections were analysed and patients presenting with acute respiratory distress were observed to be significantly more in P. vivax infections [p = 0.010; OR 2.273 (95% CI 1.76 – 2.93)]. Among haematological parameters, MCHC was found to be significantly lower in P. falciparum when compared to P. vivax. No derangement of blood parameters were significantly associated with P. falciparum or P. vivax infection. 3.3 Sub group analysis for patients with mixed malarial infection.

Results

3.1 Demographic and clinical Characteristics of study population.

Table 1: Demographics, comorbidities and other patient characteristics (N= 403) (%).

	Overall	Severe	Non Severe	P value
Age (years; mean ± SD)	35.8 ± 14.86	37.2 ± 15.09	35.5 ± 14.80	-
Male sex (n,%)	340 (84.4)	69 (79.3)	271 (85.8)	-
Origin (n,%)				
Udupi	245 (60.7)	47 (54)	198 (62.7)	-
Karnataka	117 (29)	34 (39.1)	83 (26.3)	-
Other states	41 (10.1)	6 (6.9)	35 (11.1)	-
Comorbid conditions (n,%)				
Type 2 diabetes mellitus	9 (2.2)	3 (3.4)	6 (1.9)	0.413
Chronic renal dysfunction	3 (0.7)	1 (1.1)	2 (0.6)	0.519
Carcinoma/ metastasis	3 (0.7)	2 (2.3)	1 (0.3)	0.119
Previous history of malaria	27 (6.7)	7 (8.0)	20 (6.3)	0.571
Plasmodium infection (n,%)				
P. falciparum	196 (48.6)	39 (44.8)	157 (49.7)	-
P. vivax	189 (46.9)	42 (48.3)	147 (46.5)	-
Mixed Infection	18 (4.5)	6 (6.9)	12 (3.8)	-
Duration of Stay in hospital (days; mean ± SD)	4.8 ± 2.42	6.08 ± 3.78	4.53 ± 1.74	<0.001*
Duration of fever (days; median, IQR)	5.6 (3,7)	5 (3,7)	4 (3,6)	0.024*
Improved outcome (n,%)	402 (99.7)	86 (98.8)	316 (100)	-
Total	403	87	316	

Table 2: Clinical and laboratory characteristics in severe malaria N = 81.(%)

	P. falciparum	P. vivax	p
Age (years; mean ± SD)	35 ± 14.8	36.5 ± 15.8	-
Male sex (n,%)	30 (76.9)	34 (81)	0.656
Duration of Stay in hospital (days; median, IQR)	5 (4, 8)	5 (3.7, 7)	0.355
Duration of fever (days; median, IQR)	6 (3, 7)	5 (3, 7)	0.299
Previous history of malaria	6 (15.4)	0 (0)	0.010*
Improved outcome (n,%)	39 (100)	42 (100)	-
Severe anaemia (Hct<15% or Hb<5 mg/dL)	21 (53.8)	19 (45.2)	0.508
Renal impairment (Urine output<400ml/ 24 hours and S. Creatinine >3mg/dL despite adequate volume repletion)	0 (0)	1 (2.4)	1
Hypoglycaemia (RBS < 40 mg/dL)	0 (0)	3 (7.5)	0.242
Jaundice (bilirubin> 3 mg/ dL; n,%)	18 (46.2)	21 (50)	0.729
Hepatomegaly (n, %)	13 (33.3)	9 (21.4)	0.229
Splenomegaly (n, %)	10 (25.6)	6 (14.3)	0.2
Impaired consciousness (rousable mental condition)	4 (10.3)	6 (14.3)	0.739
Repeated generalised convulsions (>3 convulsions within 24 hours; n, %)	0 (0)	1 (2.4)	1
Pulmonary Edema (Radiological evidence and lung injury score; n, %)	1 (2.6)	6 (14.3)	0.110
Acute respiratory distress syndrome (Respiratory rate >30/min or O2 saturation < 92%; n,%)	2 (5.1)	9 (21.4)	0.05*
Circulatory collapse (algid malaria) (SBP <70 mmHg; n, %)	1 (2.6)	5 (11.9)	0.203
Leukopenia (<4000/µL; n,%)	6 (15.4)	9 (21.4)	0.484
Leucocytosis (>10,000/µL; n,%)	2 (5.1)	3 (7.1)	1
Absolute neutrophil count (109/µl; median, IQR)	2.8 (1.2, 6.8)	2.9 (1.5, 4.9)	0.833
MCV (fl; median, IQR)	82.8 (80.4, 92.6)	85.1 (81.6, 91.5)	0.359
MCH (pg/cell; median, IQR)	28.1 (26.6, 30.2)	29 (27.9, 31)	0.097
MCHC (g/dL; median, IQR)	33.1 (32, 34.5)	33.8 (33.4, 34.5)	0.006*
RBC (1012/L; median, IQR)	3.8 (3.0, 4.7)	4.1 (3.5, 4.7)	0.312
Platelets (104/L; median, IQR)	6 (3.3, 13.2)	5.8 (3.0, 8.9)	0.419
S. Potassium (mmol/L; median, IQR)	4.2 (3.8, 4.6)	4.1 (3.8, 4.5)	0.412
Plateletcrit(/µl; median, IQR)	0.05 (0.03, 0.12)	0.05 (0.02, 0.09)	0.172
Total	39	42	

*p<0.05, Statistically significant.

Coinfection with P. falciparum and P. vivaxwas diagnosed in 4.5% (18/403) of study population,as presented in table 3. All patients with mixed infection had an improved outcome. No cases with history of acute renal impairment, G6PD or hypotension (systolic BP <80mmHg) were identified.Majority of cases (72.2%) were managed by artesunate–sulfadoxine–pyrimethaminealong with primaquine after microscopic confirmation of diagnosis.

Discussion

India and other south east Asian countries have committed to eliminate malaria by 2030.[3] This is a challenging goal as P. falciparum and P. vivax burden varies across India.[12,13] The state of Karnataka reports an annual parasite index of 1-2/1000 population for P. vivax and a parasite index of <1/1000 population for P. falciparum.[13]

Table 3: Demographics, comorbidities and other characteristics among patients with mixed malaria infection. (N = 18)

	N (%)
Age (years, mean ± SD)	38.8 ± 15.12
Males : Females	3.5:1
Duration of Stay in hospital (days, mean ± SD)	4.6 ± 2.09
Severe Malaria (n, %)	6 (33)
Previous history of malaria (n, %)	1 (5.6)
Improved Outcome (n, %)	18 (100)
Clinical features	
Duration of fever (days; median, IQR)	5 (3.7, 8.5)
Anemia (Hb<7 mg/dL; n,%)	5 (27.8)
Jaundice (bilirubin > 3 mg/dL; n, %)	1 (5.5)
Hepatomegaly (n, %)	4 (22.2)
Splenomegaly (n, %)	3 (16.6)
Laboratory parameters	
Hb (mg/dL)	11.6 ± 1.9
WBC (x 10 3 /uL; median, IQR)	5500 (3700,6200)
Random Blood Sugar (mg/dL)	153 ± 59.2
Absolute neutrophil count (/µl; median, IQR)	2.8 ± 0.76
MCV (fl; median, IQR)	83.1 ± 7.34
MCH (pg/cell; median, IQR)	27.8 ± 2.67
MCHC (g/dL; median, IQR)	33.3 ± 0.87
RBC (/µl; median, IQR)	4.08 ± 0.47
Platelets (x103; median, IQR)	6.2 (3.3, 8.9)
S. Potassium (mmol/L; median, IQR)	4.08 ± 0.61
Plateletcrit(/µl; median, IQR)	0.06 (0.3, 0.8)
Choice of management	
Artesunate + Primaquine(n, %)	13 (72.2%)
Quinine + Primaquine + Artemether + Lumefantrin (n, %)	1 (5.6%)
Artesunate + Primaquine + Artemether + Lumefantrin (n, %)	2 (11.1%)
Chloroquine + Primaquine (n, %)	2 (11.1%)

Although malaria control measures impact both P. falciparum and P. vivax malaria, P. vivax remains difficult to control in urban areas due to complex epidemiology and clinical presentations.[13] In present study, hospital admission details of severe malaria patients were analysed; severe cases were admitted for a significantly longer duration of 6.08 ± 3.78 days ($p < 0.001$). These cases also had a longer duration of fever ($p < 0.024$) on admission when compared to patients presenting with non-severe malaria.

The above mentioned factors may be explained by higher parasitaemia usually seen in patients presenting with severe malaria, regardless of the infecting species.

P. falciparum attributed to 48.6% (196/403) of malaria cases and 46.9% (189/403) to P. vivax. Mixed infections were observed in 4.5% (18/403) patients during the study period. These results corroborate the reports of shift in the dominant infecting Plasmodium species in India, from P. vivax to P. falciparum.[14] However there are large regional differences in the epidemiology of malaria in India. An apparent increase in cases of falciparum malaria in present study can be attributed to the fact that i) such patients require frequent hospitalisation, ii) monovalent RDTs are used for diagnosis in the primary care setup and iii) that mixed infections showed a slightly more pronounced manifestation than P. vivax malaria, as seen in some other studies.[15,16] Interestingly, on analyzing severe cases, the majority were attributed to P. vivax accounting for 48.3% (42/87). This observation has been reported over the years from endemic regions of vivax malaria.[17] Maguire JD et. al. have highlighted and have cautioned against severe forms of vivaxmalaria in tropical areas such as our study region.[18,19] On analysis of previous admissions, repeat infection of an unknown malarial parasite in a 6 month interval were more likely to be found in P. falciparum [$p = 0.010$; OR 2.273 (95% CI 1.76 – 2.93)]. This suggests that there may be either inadequate management of the initial infection at the primary healthcare centre or repeat infection due to high vector burden in study region. This finding may also be due to some amount of misdiagnoses of mixed malarial infections at the primary level due to dependency on microscopy and RDTs.[14] On analysis of severe malaria cases, severe anaemia followed by jaundice were the most common presentations irrespective of infecting species. Significant association between acute respiratory distress syndrome and P. vivax infections was observed [$p = 0.05$; OR 0.198 (95% CI 0.04 – 0.98)].

Respiratory dysfunction has been reported from other studies done from similar study regions, however its association with P. vivax is unclear.[7] Val et. al. suggested that similar to P. falciparum infection, P. vivax may also demonstrate sequestration of parasitized red blood cells in the pulmonary vasculature.[20] No cases of severe thrombocytopenia, disseminated intravascular coagulation (DIC) or abnormal bleeding were observed in present study. These findings differ from the most prevalent severity signs associated with vivax malaria including, severe thrombocytopenia, Circulatory collapse/ shock and hepatic dysfunction.[21] Some clinical characteristics, comorbidities and manifestations as

mentioned in the patient case files, e.g., impaired consciousness without continued Glasgow Coma Scale (GCS) monitoring and hypotension without evidence of decreased perfusion, may have caused an overestimation or underestimation of severe malaria and remains a limitation of present study.

Furthermore, parasitemia levels in study population are lacking as only reports of >10,000 parasites/µl have been noted in patient medical records with specific request from admitting physicians. In fact, the lack of data on outpatient malaria contributes to an inaccurate presentation of the overall patients with confirmed malaria diagnosis. Differences in severity presentations with respect to suspected infecting Plasmodium spp. are important for the management and diagnosis of malaria. The above observations suggest that WHO definitions, largely based on severe falciparum malaria, may require revisions to include varying clinical presentations of vivax or mixed malarial infections.[7,9] Comparing of laboratory parameters, leukopenia or leucocytosis was not found to be significantly associated with severe vivax malaria ($p = 0.484$, $p = 1$), this finding is comparable to a study by Kotepui et. al. where only patients with very high parasitaemia (>10 parasites/oil field) tended to have higher leukocyte counts.[16] Our study found no significant associations between haematological parameters of severe malaria on the basis of infecting Plasmodium spp.

A subgroup analysis was performed for 18 (4.5%) patients with mixed P. falciparum and P. vivaxinfection. Mixed malarial infections have been reported in up to 13% of total infections with an increased prevalence in middle and southwest coast of India.[14] Majority of the patients were young, 38.8 ± 15.12 years of age and were male (77.8%). This demographic is considered the major contributor to the Indian workforce. Patients were admitted for an average of 4.6 ± 2 days, which highlights the necessity of prolonged inpatient stay for patients with mixed infections. In our study, mixed malaria infection were not confirmed using molecular methods, and diagnosis was based on microscopy and rapid assays. This has shown to underestimate the burden of mixed infection in endemic regions.[7,14] The sensitivity, when compared to PCR, of RDTs when diagnosing mixed malarial infections is 58.3% and with microscopy is only 16.6%.[22] RDTs in India are limited by poor sensitivity and future implementation of molecular techniques are imperative for accurate diagnosis of mixed infections. Rise in reports of mixed malarial infections have also been linked to changing climate conditions along with increasing migration, urbanisation and globalisation in tropical regions.[23]

Therefore, diagnosis and appropriate management for mixed malarial infections are paramount when considering elimination goals. Furthermore, the chance of recurrence in mixed malaria cases due to P. vivax must be considered when implementing appropriate treatment and control measures. Majority of mixed malarial infection were managed with artemisinin derivatives or quinine along with primaquine. There were no fatalities reported in study population. Our study suggests, attributing severe malaria to P. falciparum or P. vivax alone can be misleading especially in regions with complicated epidemiology, like India. Furthermore, in mixed malarial infection diagnosis, presentation and management requires multidisciplinary attention from clinical, laboratory and community perspectives. Research addressing clinical and laboratory manifestations in malaria endemic zones remain essential to maintaining a robust and validated database to help establish clear recommendations for malaria elimination.

Conclusion

Malaria continues to make up a significant partof the inpatient diagnosis in India and activities towards elimination are hindered by the complex epidemiology in endemic regions like coastal Karnataka. Attributing severe malaria to P. falciparum or P. vivax alone can be misleading especially in such regions. Furthermore, identification of malarial coinfections are difficult without molecular diagnostic tools. Laboratory aid in diagnosing mixed malarial infections is paramount in selecting appropriate antimalarial therapy and ensuring health and safety of the patient.

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Original Article

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Immuno Histomolecular Profile in Periampullary Adenocarcinoma : A Clinico-Pathological Study

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Abstract

Periampullary adenocarcinomas (PAC) are rare malignant tumors with worst survival rates due to destructive route of the disease. It comprises distal bile duct, pancreatic, ampullary and duodenal adenocarcinoma that originate within periampullary complex. The primary origin of PAC in this area is often difficult previous to the surgery into pancreaticobiliary (PB-PAC), intestinal (I-PAC) and mixed type (MT-PAC) as PB-PAC carries bad prognosis.

Objective: The main aim was to study the histomorphological features and immunohistochemical (IHC) expression of Cytokeratin (CK) 7 and 20 in PAC and assess their expression with known histopathological prognostic parameters.

Method: A total number of 31 resected pancreatoduodenectomy specimens were studied in the department of Pathology, in a tertiary care center, Karnataka, India for histomorphological features with CK7 and CK 20 expression. All the statistical methods were carried out through the SPSS for Windows (version 22.0). A p-value of ≤0.05 was taken to be statistically significant.

Results: The cases were categorized into PB-PAC (CK7+), I-PAC (CK20+) and MT-PAC (CK7+ and CK20+) based on histomorphological and histomolecular typing. There was a positive association between histomorphology and histomolecular typing. The difference in the proportion of histomolecular profiling between the expressions was statistically significant with p-value of ≤0.001.

Conclusions: The concordance in PB-PAC, I-PAC and MT-PAC by usual haematoxylin and eosin microscopy and later confirmed by the immunophenotyping advocates sub typing to be incorporated in the routine histopathology report. The importance of correctly categorizing of the PB-PAC, I-PAC and MT-PAC is mainly for the prognosis and difference in administering of the targeted chemotherapy regimens.

Key Words: Adenocarcinoma, CK7, CK20, Pancreaticobiliary, Periampullary region.

Introduction

Periampullary adenocarcinomas (PAC) are rare malignant tumors that originate within periampullary complex having a common embryologic source from the foregut. It comprises distal bile duct, pancreatic, ampullary and duodenal adenocarcinoma with worst survival rates due to destructive route of the disease. It accounts for less than 1% of all the gastrointestinal tumors. Although these tumors have different origins, the complex regional anatomy dictates a common pancreatoduodenectomy operative approach. Since it is a transition area connecting the biliary tract ductal epithelium and intestinal epithelium, the primary origin of PAC in this area is often difficult previous to the surgery into pancreaticobiliary (PB-PAC), intestinal (I-PAC) and mixed type (MT-PAC)[1,2]. The final diagnosis of histological subtype is very important along with the degree of tumor differentiation, perineural

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infiltration (PNI), lymphovascular invasion (LVI), margin status, resected lymph node status which significantly influences the outcome and different chemotherapy regimens[3,4].

The histologic subtyping of PAC into pancreaticobiliary (PB-PAC) and intestinal (I-PAC) according to Albores-Saavedra[5] is emerging as an important prognostic factor[6,7]. This classification is associated with histolpathological features which influence the overall survival, as PB-PAC type is associated with lower survival rates, when compared to good prognosis of I-PAC type[1,7-10].

Thus, the methods used to classify these tumors should be more objective and reproducible to control inter observer variability. Several studies have classified PAC subtypes using the morphologic criteria in combination of a panel of immunohistochemistry (IHC) markers[2,6,11].

CK7 and CK20 are reliable and well characterized IHC markers, and are helpful in distinguishing PB-PAC and I-PAC type respectively[2,6,10,12-14]. Data on chemotherapy options for patients with the separate periampullary subtypes are very limited but do support the conception that treatment should be tailored according to the histological subtype[15].

This study is taken up to know the histomorphological features with immuno histochemical expression of CK7 and CK20 in PAC, and its association with histopathological subtyping, grading and staging.

Materials and Methods

The material for the present study was undertaken in the department of Pathology, in a tertiary care center, Karnataka, India. Ethical clearance was obtained by the University ethical committee. A total number of 31 resected pancreatoduodenectomy specimens (Whipple's procedure) were studied for five years. All cases diagnosed histopathologically as adenocarcinomas of the periampullary region in resected specimens of pancreatoduodenectomy were included.

All specimens (Sep2017-Aug2019) were received in 10% of neutral buffered formalin and relevant clinical information was obtained as per the proforma. The specimen was kept for fixation for 24-48 hours. The grossing was done according to the recent 2017 CAP protocol[16] and the most representative tumor bits and other bits were taken for histopathological processing. Deparaffinised sections were stained with haematoxylin and eosin (H&E). The tumors were classified according to WHO classification[17]. Tumor (T), Node(N) and Metastasis (M) cancer staging system of the American Joint Committee of Cancer (AJCC), eighth edition[16], was followed for staging of the PAC specimens.

All the tumors were classified into PB-PAC, I-PAC and MT-PAC type according Albores-Saavedra[5] microscopic features (Table 1).

Tables with legends

Table 1: Microscopic features of pancreaticobiliary and intestinal type of periampullary adenocarcinoma.

Pancreaticobiliary	Intestinal type
The individual neoplastic glands are small ,simple branching glands, arranged in complex – papillary and micropapillary pattern.	The individual neoplastic glands are well-formed tubular glands , complex branching, arranged in cribriform and nest pattern
The lining neoplastic epithelium is cuboidal to low columnar type in a single layer	The lining neoplastic epithelium is tall columnar with cytoplasmic mucin.
Nucleus–round with marked atypia and lack pseudo stratification	Nucleus–elongated oval or cigar shaped with moderate atypia and pseudostratified
No goblet cells	Well differentiated goblet cells
Mild Necrosis	Abundant luminal necrosis
Abundant and extensive desmoplastic stroma	Mild desmoplastic stroma

All diagnostic tumor slides were re-reviewed and the most representive block was selected for cytokeratin immunochemistry CK7 (FLEX Monoclonal Mouse Anti-Human Cytokeratin 7,Clone OV-TL 12/30) and CK20 (FLEX Monoclonal Mouse Anti-Human Cytokeratin20,CloneKs20.8) to identify PB-PAC and I-PAC sub type respectively in all the 31 cases.

3-4 µm thick sections were taken on two separate Poly-L-Lysine coated slides and air dried. The slides were baked at 60° C for 1 hour in hot air oven. Slides were deparaffinized, rehydrated and heated in a pressure cooker containing antigen retrieval solution, sodium citrate buffer at pH 6. 1 liter of retrieval solution was brought to boil in the pressure cooker. Slides were placed in metal staining racks and lowered into pressure cooker ensuring that the slides were completely immersed in the retrieval solution. When the pressure cooker reached operating temperature and pressure, it was timed for 1 minute or up to 2 to 3 whistles. The pressure cooker was removed from the heat source and cooled by placing it under running cold water with the lid on. The slides were cooled, washed

with water and buffer solution. Peroxide block was applied for 10 min and washed with Trisbuffered saline (TBS) twice for five minutes. Protein block was applied for 10 min and washed with TBS twice for five minutes.The sections were incubated with primary antibody CK 7 and CK 20 for 1 hour and washed with TBS twice for five minutes. Post primary block/enhancer was applied for 30 min and washed with TBS twice for five minutes. The sections were incubated with SS label (polymer) for 30 minutes and washed with TBS twice for five minutes.

The bound antibody was visualized using a DAB-chromogen substrate which was prepared by adding 50 µl of DAB chromogen to 1 ml of DAB buffer. The sections were rinsed in running water and counter stained with hematoxylin and again rinsed in water for five minutes. External positive control tissue included sample of pancreatic tissue with a diffuse CK7 positivity for CK 7 marker and sample of normal intestinal mucosa with a diffuse CK 20 cytoplasmic immunoreactivity for CK 20 marker was taken. The negative control for CK 7 and CK 20 were taken in the selected slides which were treated with tris-buffer solution alone without the primary antibody.

The cytoplasmic membrane brown color staining was taken as positivity for CK 7 and CK 20. The staining intensity of each IHC reaction were scored semi quantitatively[12, 18].

- No staining reaction or <10% positively stained tumor cells = 0,
- 10-50%=1, 51-90%=2and 90%=3.

Scores 0 were regarded as negative and Scores 1-3 were regarded as positive. All the tumor were classified into PB-PAC where CK 7 is Positive (Fig 1a, b & c), as I-PAC when positive for CK 20(Fig 1d, e & f), and MT-PAC were both CK 7 and CK 20 are positive (Fig 1g, h & i). After compiling of H&E and IHC data then final histomolecular diagnosis was reported.

Statistical Analyses

All the statistical methods were carried out through the SPSS for Windows (version 22.0). A p-value of ≤0.05 was taken to be statistically significant. Descriptive statistics, Chi-Square Test, Independent-Samples T Test, Contingency coefficient analysis (Crosstabs), and One-Way ANOVA test were used to know the association.

Results

A total of 31 cases were included in this study with clinico-pathological features (Table 2). The mean age of 59.32(±9.93) years, female predominance and jaundice as the most common presenting complaint were noted. The maximum size of the tumor documented was 7cm and minimum was 1cm, with a mean tumor size of 2.74 cm and largest size was seen in PB-PAC.

Table 2: Clinico-Pathological features in 31 cases of periampullary adenocarcinoma.

1	Age	38-75 years, Mean age: 59.32 (±9.93) years			
2	Male: Female	1:1.066			
3	Presenting complaints	Jaundice (83.87%)			
4	Mean total bilirubin	8 mg/dl			
5	Mean tumor size	2.74 cm			
6	Histopatho logical type	Total	PB	I	MT
		31	19 (61.3%)	07 (22.6%)	05 (16.1%)
7	Histopatho logical grade	Total	PB	I	MT
	Grade 1	1 (3.2%)	00	01	00
	Grade 2	27(87.1%)	17	05	05
	Grade 3	3 (9.7%)	02	01	00
8	Lymphovascu-lar invasion	Total	PB	I	MT
	Present	12(38.7%)	07	03	02
	Absent	19(61.3%)	12	04	03
9	Perineural invasion	Total	PB	I	MT
	Present	04(12.9%)	01	02	01
	Absent	27(87.1%)	16	07	04
10	pT Stage	Total	PB	I	MT
	T1B	2(6.5%)	01	01	00
	T2	21(67.7%)	15	02	04
	T3A	1 (3.2%)	01	00	00
	T3B	7 (22.6%)	02	04	01
11	pN Stage	Total	PB	I	MT
	Nx	2 (6.5%)	02	00	00
	N0	17(54.8%)	10	05	02
	N1	8 (25.8%)	05	01	02
	N2	4 (12.9%)	02	01	01

On H&E staining, PB-PAC type 19 (61.3%) was the most common tumor encountered followed by I-PAC type 07 (22.6%) and MT-PAC type 05 (16.1%). Maximum cases were Grade 2 (moderately differentiated).LVI was seen in 12 cases (38.7%) and PNI was seen in 4 cases (12.9%). There were 67.7% of T2 category, and 54.8% of N0 category (Table 2).

The IHC staining revealed CK7 was positive in 22 cases (71%) and negative in 09 cases (29%)

whereas CK 20 was positive in 14 cases (45.2%) and negative in 17 cases (54.8%). After the IHC markers CK 7 and CK 20, all 31 cases were classified as follows: 17 cases (54.8%) of PB-PAC, 9 cases (29%) of I-PAC and 5 cases (16.1%) of MT-PAC (Table 3). According to the staining intensity of each IHC reaction(Fig 2a), the CK 7 and 20 showed maximum in with grade 2 intensity.

PB- Pancreaticobiliary, I-Intestinal, MT-Mixed

The Correlation of various prognostic parameters with histomolecular diagnosis was as follows: PB-PAC showed maximum cases with grade 2(Fig 2b), 07 cases with LVI and 01 case of PNI (Fig 2c), higher pT staging with T2 and pN staging with N1 (Fig. 2d). In the final pTNM staging of PAC, there were fewer cases in higher staging indicating an early presentation. There was a positive association between histomorphology and histomolecular typing (Table 3). The difference in the proportion of histomolecular profiling between the expression was statistically significant with p-value of 0.0001(Table 4).

Table 3: Concordance relation between Histopathology and IHC diagnosis of periampullary adenocarcinoma. PB-Pancreaticobiliary, I-Intestinal, MT-Mixed.

Histopathologial Type		Final Histomolecular diagnosis			Total
		PB (CK7+)	MT (CK7+ & CK20+)	I (CK20+)	
PB	Count	16	1	2	19
	%	94.1%	20.0%	22.2%	61.3%
MT	Count	1	4	0	5
	%	5.9%	80.0%	0.0%	16.1%
I	Count	0	0	7	7
	%	0.0%	0.0%	77.8%	22.6%
Total	Count	17	5	9	31
	%	100.0%	100.0%	100.0%	100.0%

Table 4: One way ANOVA table to compare the means of CK7 and CK20 between the groups.

		Sum of Square	Degrees of Freedom(df)	Mean Square	F	Sig.
CK_7_score	Between Groups	32.019	2	16.009	59.535	.0001
	Within Groups	7.529	28	.269		
	Total	39.548	30			
CK20_score	Between Groups	35.115	2	17.558	103.377	.0001
	Within Groups	4.756	28	.170		
	Total	39.871	30			

This study shows the concordance between routine H&E microscopy and immuno phenotyping of CK 7 and CK20.The concordance in PB-PAC type was 94%, I-PAC type was 100% and MT-PAC type was 80% which means these respective percentages of the cases were identified correctly by routine H&E microscopy and later confirmed by the immunophenotyping. There were cases which were reclassified by immunopheno typing but they represented only a small part of the sample. These reclassified cases belonged to the category of PB-PAC and MT-PAC (Table 3). The cases were followed up for 3 months to 3 years in the present study. The expired patients were encountered maximum in PB-PAC type suggesting the least survival over 3 months to 3 years.

Discussion

PAC was anticipated epidemiologically as the 7th cause of mortality by cancer worldwide in 2014. Many studies explain that it could turn out to be the 2nd leading cause of cancer deaths by 2020 and that its prevalence is rising in the developing countries since the relocate of risk factors like smoking , obesity, poor eating habits, and sedentary lifestyle[18].

The tumors associated with periampullary region presents early in due course of disease due to obstruction to the flow of bile, but there is an overall wide range of outcomes associated with these PAC. The prognosis mainly depends on the histomolecular subtypes and whether presence or absences of known prognostic parameters like lymph node status, LVI, PNI, surgical margins, advanced tumor stages (pT3-4) and distant metastasis[2,3,15]. In our study, we found peak involvement of fifth decade which was seen even in all the previous studies[6,10,13,18-30]. In majority of the studies, the male preponderance is known. In our study, we found female preponderance and this correlated with studies by Ferchichi et al[18] Yun S et al[19], Moriya et al[20] and Aloysius et al[21], which ranged from 1:1.056 to 1:1.29. This can be due early awareness among the female or due to the small sample size. The jaundice was the main presenting complaint in our study and 32.3% cases presents with more than 10 mg/dl of total bilirubin as in the many of the studies done[22.23]. This is mainly due to the destructive course of the tumor and causes obstruction to the bile duct leading to jaundice. In our study, the mean tumor size was 2.74 cm which involved the periampullary region as a whole. Thus, the anatomical classification like Intra-ampullarypapillary-tubular neoplasm with invasion (Intra-AMP), Ampullary-ductal, Periampullary-duodenal and Ampullary-not otherwise specified (NOS) was not possible as like in the other studies[18,19,24-27].

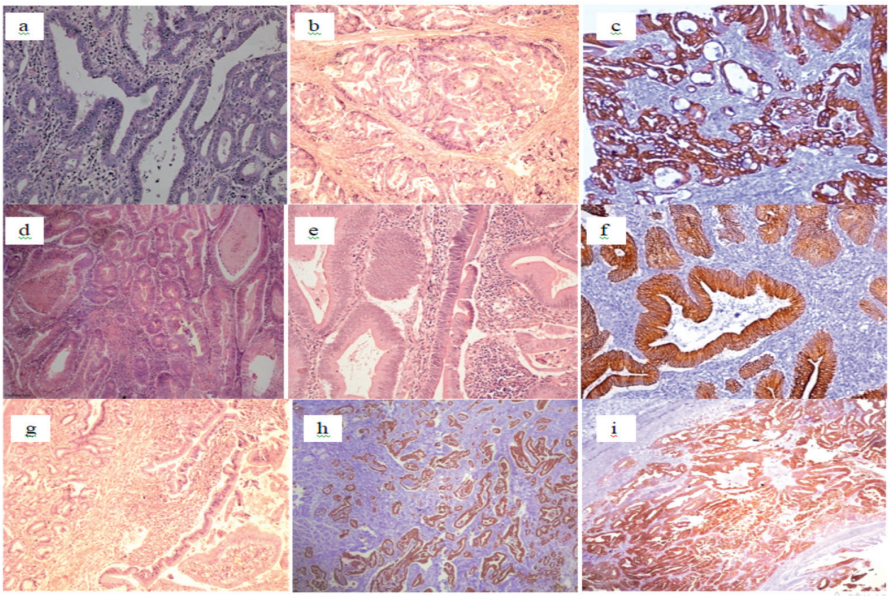

Fig. 1: Microscopic Features of Periampullary Adenocarcinomas.

a) Pancreaticobiliary type with small, well-formed glands with minimal luminal necrosis and no pseudo stratification (H&E, x100). b) Pancreaticobiliary type with desmoplasia - (H&E, x100), c) IHC of pancreaticobiliary type CK 7 positive (IHC, x40). d) Intestinal type with abundant luminal necrosis with minimal desmoplasia (H&E, x100). e) Intestinal type with tall columnar cells and pseudo stratification (H&E, x200). f) IHC of intestinal type CK 20 positive(IHC,x200). g) Mixed type having features of pancreaticobiliary and intestinal type (H&E, x40). h) IHC of mixed type CK 20 positive (IHC, x20). i) IHC of mixed type CK 7 positive (IHC, x40).

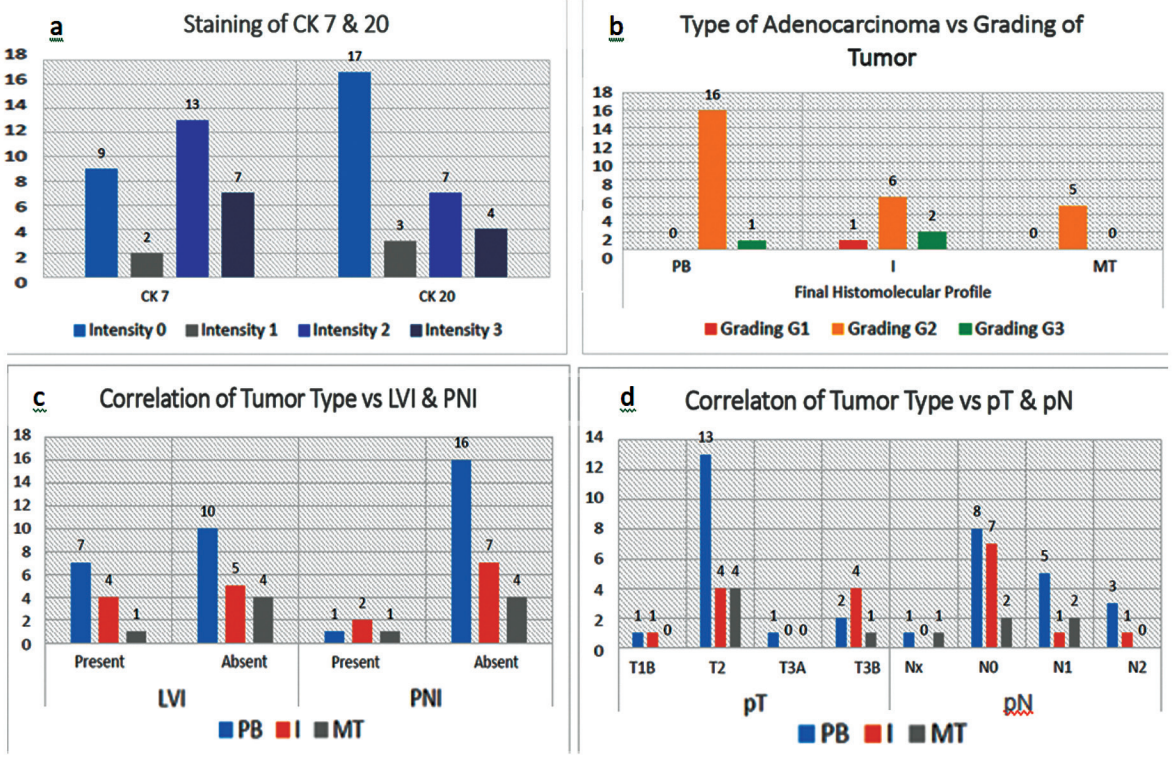

Fig. 2: Correlation of final histomolecular diagnosis of periampullary adenocarcinomas with various known prognostic factorsrevealing that pancreaticobiliary type associated with overall poor prognosis.

a) IHC intensity of CK7 & CK20. b) Grading of tumors. c) LVI and PNI correlation. d) Correlation with pTNM staging-pT & pN. PB-Pancreaticobiliary, I-Intestinal, MT-Mixed, LVI-Lymphovascular invasion, PNI-Perineural invasion.

The majority of the studies[6,9,13,18,19,23,26-29] showed the predominance of the PB-PAC. This correlated with the findings of this study and thus, states that the PB-PAC predominates over the other type of adenocarcinomas of the periampullary region as described under WHO Classification[17].

Histopathological grading correlated with Aloysius M et al[21] and Perysinakis et al[23]and showed the predominance of moderately differentiated type of PAC. There were few cases with LVI and majority of cases showed no PNI seen. All these findings suggest that the patients presented early in the due course of the disease as seen in other studies also.

Lymph node metastasis is considered as one of the most independent prognostic markers in the PAC. In our study, we found majority of the cases showed no metastasis to the lymph node leading to better prognosis and thus improvement in morbidity and mortality of the patients. This is mainly due to the early presentation of the cases, majority with moderately differentiated tumor, less LVI and PNI incidence. There was predominance of T2 tumors in the present study and only few cases with the lymph node metastasis which correlated with other studies[10,26,30,31].

As in many studies[10,13,15,19,23,28] there was a positive association between histomorphology and histomolecular typing. The difference in the proportion of histomolecular profiling between the expressions was statistically significant (p-value -.0001) in our study. This shows the concordance between routine H&E microscopy and immunophenotyping of CK 7 and CK 20 (Table 3). There were cases which were reclassified by immunophenotyping.

These reclassified cases belonged to the category of PB-PAC and MT-PAC type which was also seen in the previous studies [6,10,30,31]. So, if strict histopathological criteria are followed (Table 1) according to Albores-Saavedra[5] the subtyping can be done on H&E alone also and this will also reduce the interobserver variability[15,32-35]. Thus, proving the importance of histopathological features as a helpful diagnostic tool in correctly subtyping of PAC even if IHC is not used especially in poor socio economical status.

The PB-PAC showed the maximum cases with moderately and poorly differentiated tumors i.e. 94.1% and 5.9% respectively. PB-PAC also showed maximum cases with high T staging with T2 and T3 Staging i.e. 76.5% and 17.7% of cases respectively with higher number of cases with node positivity. All these are well documented prognostic markers which affect the patients directly and thus deducing that PB-PAC have worst prognosis (Fig 2).

Thus, the importance of correctly categorizing of the PAC into PB-PAC, I-PAC and MT-PAC is mainly due to the prognosis and the difference in administering of the chemotherapy regimens. There is a difference in chemotherapy response in various type of PAC. The PB-PAC may benefit from gemcitabine therapy and those with I-PAC type tumors benefit from 5-fluorouracil (5-FU) – based regimen[15,32]. Overall, the PB-PAC type has the poor prognosis and presents early with the lymph node metastasis which is confirmed in this study. In this perspective, histopathology reports should be consistently mentions all these factors in the pancreatoduodenectomy specimen.

Attempts to classify PAC face relatively a lot of challenges due to genetic characteristics of different subtypes remain imprecise and indistinct. Despite numerous studies, PAC stay behind with a clear lack of an evidence-based histopathologic subtype and standard care treatment of adjuvant therapy. The enhanced characterization of the different immuno histomolecular features of PAC will provide not only a better understanding of this tumor, but also the opportunity for discovering new targeted therapeutic agents[2,15,18,35].

Additional research is mandatory to explicate whether statistically and clinically significant differences be present that may demand a change in the existing adjuvant management strategies

The limitation of the study are small sample size and, the overall survival rate, progression, recurrence rate in this study was not assessed, as some of the cases were lost due to receiving of the treatment like chemotherapy at higher centers and even communication barriers.

Conclusions

Histomolecular profiling of PAC is considered superior to anatomic location of the tumor in prognosticating survival. The PB-PAC has the poor survival when compared to I-PAC type. Lymph node involvement is one of the most important independent prognostic factors in PAC. Thus it's important to differentiate these two subtypes by the help of histomorphology, IHC markers and

incorporating in the routine histopathology report.

There are various markers which can be used for the subtyping but in view of the resources, CK7 and CK20 are more economical. The categorizing of the PAC into PB-PAC, I-PAC and MT-PAC sub type minimizes interobserver variability, helps to know the prognosis and independently potentiates in administering of the targeted chemotherapy regimens especially in our country.

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Original Article

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Human Rights to Health and Equity in India with Special References To Union Territory of Jammu & Kashmir

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Abstract

Health is not merely the absence of disease but a state of physical, mental and social well-being. It encompasses all facets of human right, including the right to health automatically. In the erstwhile Jammu and Kashmir state and now Indian Union Territory (UT) has been under conflict situation resulting in assaults on health by conventional and rubber bullets, tear gas shells and pellet firearms in crowd control and security. The security forces during the last three decades to quell the discontentment and uprising have used power to the detriment of the people's health and well being. The access to health care and delivery assumes importance in conflict and peace situations equally being inalienable human right to life and health. The paper takes a legal stance on security-driven health issues and diseases in the human rights perspective in Kashmir.

Keywords: Physical Health; Mental Health; Conflict Situations; Human Rights; Emergency Preparedness.

Introduction

The human rights to health mean physical, mental and spiritual health.[1] The access to medical services, sanitation, food, housing, healthy working conditions and the environment is inclusive to the concept of the right to health.[2] The Supreme Court in Vincent Panikulangara v. Union of India,[3] observed that the 'maintenance and improvement of public health deserve top priority and indispensable to individual, community and society.' Article 47 of the Constitution of India, 1950 recognizes nutrition security, the standard of living,[4] and improvement of public health as the paramount principle of governance. In Consumer Education and Resource Centre v. Union of India,[5] the Supreme Court envisaged that 'the right to health and medical care' metaphor in the vocabulary of fundamental and human right.[6] The judicial interventions under Article 21 of the Constitution of India, 1950 witnessed streak of health entitlements in normal and epidemic-pandemic situations.[7] However, the use of force by security personnel, curfew and lockdown in conflict situations in the union territory of Kashmir in India led to depression, anxiety and PTSD and gross violation of health-related human right.[8] The health care system must be guided by human rights standards, which ordain that everyone must have access to health care under public health law and governance.[9] The human right to health care means that hospitals, clinics, medicines, and doctors' services must be accessible for everyone on an equitable basis for the public good. According to human rights organizations and media reports,[10] people with chronic diseases such as diabetes, epilepsy, heart ailments, and liver and kidney failures are finding it extremely challenging to reach health-care units under curfews, strikes and cessation of information system. Sometimes ambulances are frisked and held up having a detrimental effect on patient and treatment.[11] Recently, members of the security forces made a pregnant woman in her last stage of birth walk about 6 km to reach a hospital.[12] The

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high frequency of penetrating eye injuries among young adults (nearly 75% of the injuries occurred below 23 years of age underscores the economic and social costs of ophthalmological trauma.[13] The paper is devoted to the health-related human rights violations in conflict situations in the Union Territory of Kashmir in India.

Material & Methods

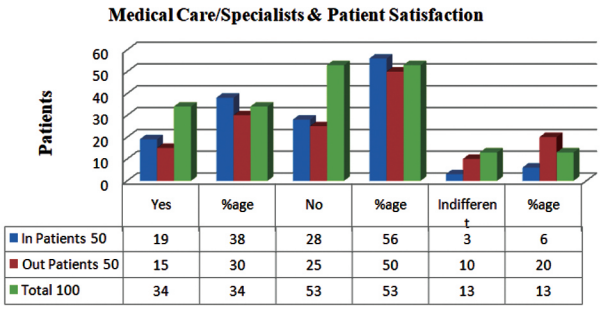
The material and methods for the study include the analytical method of legal research by undertaking the legislative survey and scrutiny of health and human rights laws at international, national, state and regional levels.[14] It also employs Brint and Williams' pragmatism along with the health behavioral and determinants approach[15] in socio-legal context of Union Territory of Jammu and Kashmir care system, health delivery services, patient satisfaction and utility, doctor–patient relationship.[16] The empowerment for the right to health and 'most significant change' (MSC) methodology employed in measuring the impact of state interventions to foster understanding in conflict situation of Union Territories of Jammu and Kashmir.

The MSC methodology applied in the Philippines, Palestine, Congo, and El Salvador between 2010 and 2013 to observe a significant change in the realization of the human right to health.[17] The comparative study of human rights laws and health in Kashmir based on international conventions, federal rules adopted by the nation through various conventions and India's obligations to protect the rights to life and health, enabled by its constitution.[18] The right to health widely recognized in international human rights law. There is a plethora of laws and catena of cases to buttress the right to health in human liberty and humanitarian laws context. However the real world implementation in the context of Union Territories of Jammu and Kashmir is highly relevant in the healthy right and health equity studies.

Results

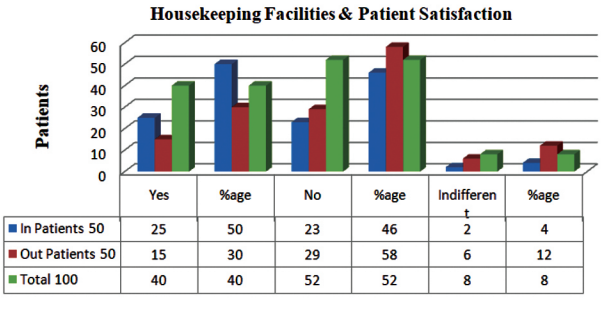
After the declaration of J&K as UT and consequential lockdown resulted in gross human rights violations by the state, the Human Rights Watch estimates revealed that more than 50,000 people had been killed there since 1989. The people of Kashmir need healing touch and no further subjugation and alienation.[19]

Health Right & Medical Care System: The health care service in Jammu and Kashmir since last three decades discerns uneven health profiling. The inadequacy of preventive and curative system is adversely affecting health equity as well as quality.[20]



	Yes	%age	No	%age	Indifferent	%age
In Patients 50	19	38	28	56	3	6
Out Patients 50	15	30	25	50	10	20
Total 100	34	34	53	53	13	13

Fig. 1: Medical Care/Specialists & Patient Satisfaction.
Source: Field Work



	Yes	%age	No	%age	Indifferent	%age
In Patients 50	25	50	23	46	2	4
Out Patients 50	15	30	29	58	6	12
Total 100	40	40	52	52	8	8

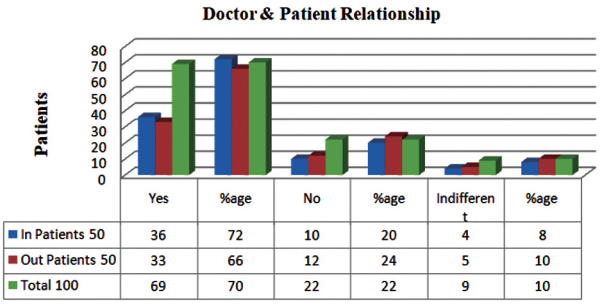
Fig. 2: Housekeeping Facilities & Patient Satisfaction.
Source: Field Work

The health care delivery system in conflict situations demands emergency preparedness which involves acute injury or illness, surgeries and trauma prevention in short and long term health effects.

The patient satisfaction is an essential and commonly used indicator for measuring the quality in health care. So far as this question is concerned, based on data received, 34% respondents said that they are quite satisfied and 53% respondents said that they are partially happy.

Therapeutic Dimension & Patient Satisfaction: This becomes a quite daunting task to meet the expectations of patients in conflict situations. Therefore when 13% of respondents said that they were not satisfied with the medical care they received, it did not surprise much to health delivery system but negates the human right to health. The housekeeping staff must have specialized knowledge specific to the health care site and unit where they work. They are required to follow complex and exacting cleaning protocols. So far as this question is concerned based on data received

40% respondents said that they are quite satisfied and majority 52% respondents said that they are partial satisfied and 08% said that they were not happy with the housekeeping facilities.

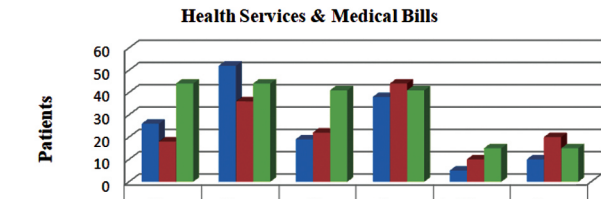


	Yes	%age	No	%age	Indifferent	%age
In Patients 50	36	72	10	20	4	8
Out Patients 50	33	66	12	24	5	10
Total 100	69	70	22	22	9	10

Fig. 3: Doctor & Patient Relationship.
Source: Field Work

The doctor-patient relationship is one those built-in terms of mutual respect, knowledge and trust. So far as this question is concerned based on data received the majority of 69% respondents says yes doctors always give their best 22% respondents disagree with the fact. Less number of respondents 09% remain indifferent related the services provided by doctors.

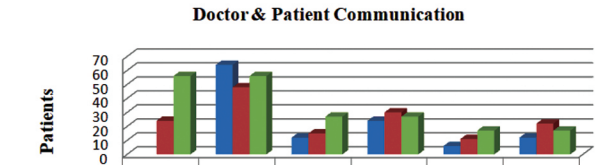
Equity & Access To Health Care: The equity and access to health care is manifested from the staggering cost and affordability by the people. The medical bill is patients responsibility, and patients have a hard time while paying their medical bills for availing medical services like registration fee, test bills and medical bills.



	Yes	%age	No	%age	Indifferent	%age
In Patients 50	26	52	19	38	5	10
Out Patients 50	18	36	22	44	10	20
Total 100	44	44	41	41	15	15

Fig. 4: Health Services & Medical Bills.
Source: Field Work

The medical bill is patients responsibility, and patients have a hard time while paying their medical bills for availing medical services like registration fee, test bills and medical bills.[21] The above table shows that bulk of 44% respondents were worried about paying outrageous medical bills. In comparison, 41% respondents were satisfied with paying their medical bills and 15% respondents didn't say anything about Medical bills.



	Yes	%age	No	%age	Indifferent	%age
In Patients 50		64	12	24	6	12
Out Patients 50	24	48	15	30	11	22
Total 100	56	56	27	27	17	17

Fig. 5: Doctor & Patient Communication.
Source: Field Work

A question put to respondents regarding showing respect and cooperation to patients reveals that 56% of respondents agreed with this fact, 27% respondent choose to disagree, and 17% of respondents were such who didn't say anything. Thus the therapeutic perception of access to medicines and health care in government hospital of Union Territories of Jammu and Kashmir remains to be seen in times to come on human right front.

Discussion

Article 12 of International Covenant on Economic, Social, and Cultural Rights (ICESCR) provides for the right to the enjoyment of the highest attainable standard of physical and mental health.[22] The right to health widely recognized in international human rights law and supported by the catena of cases. The Figure below vividly depicts the health-related human right provisions under the international and regional human rights instruments:

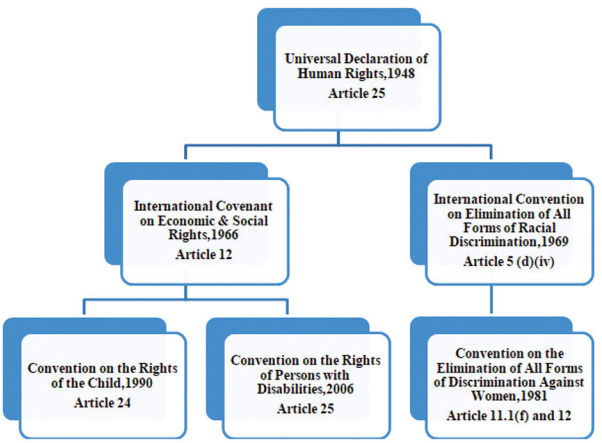


Chart 1: Right to Health Provision under Human Rights Instrument.

The United Nations, human rights mechanisms, provide that the right to health embraces a wide range of socio-economic factors that promote conditions in which people can lead for a healthy life.

Pellet Guns Induced Injuries: The violation of right to health is commonly attributed and reported by use of pellet shotguns. The pellet-firing shotguns have been responsible for blinding, killing and traumatizing hundreds of people in Kashmir. It ostensibly considered a less-lethal or non-lethal weapon is having a rubber or plastic-coated non-live rounds. That is why it is used across the world to manage agitating mobs to cause no severe injury or death. While the government projects the pellet gun hits one or two organs but a pellet damages multiple organs that too with various perforations. The Amnesty International India report on Losing Sight In Kashmir, The Impact Of Pellet-Firing Shotguns. It mentioned that 88 people eyesight damaged by metal pellets fired from pump-action shotguns used by the Jammu and Kashmir Police (JKP) and Central Reserve Police Force (CRPF) between 2014 and 2017.

A study conducted by doctors of Department of Ophthalmology at Government Medical College, Srinagar reveals that out of 604 patients, both eyes were involved in 16 (5%) patients, left eye in 48% and right eye in 47% of patients. Making a total of 636 eyes studied. The mean age of the patients was 22.5±7.73 years with a range of 5 to 59 years.[23] The use of pellet guns to control the crowds has left nearly thousands of people injured[24] and duly corroborated by studies across the world[25] and Kashmir.[26] An analysis of ocular pellet gun injuries in Kashmir showed that one-third of the survivors permanently lost their eyesight.[27] SMHS Hospital, which has received the largest number of referrals from district hospitals, reported to the media that, between July 8 and August 9, 2016, it received 933 people injured by pellets, including several who died from their pellet injuries. The hospital also treated 67 bullet injury cases, and 35 people wounded by tear gas canisters.[28]

Human Right & Mental Health Problems: The chronic violence in conflict situations has resulted in a 33% increase in mental health problems. While mental health is a now well-recognized problem in Kashmir, the medical services remain above nominal. The use of these non-lethal weapons often leads to lasting injuries, permanent disability and death.[29] Clinical studies on survivors and victims of pellet gun injuries in Kashmir show that only one-third of the injury sites were the lower limbs, the remaining affected other parts of the body with more than one-fourth hitting the head region.[30] The use of force by JK police and the CRPF against protesters in Kashmir has violated the human right to health like depression, anxiety and PTSD were significantly higher in women than men. Nearly 30% of Kashmiri adults use tobacco as a coping strategy. People suffering from stress tension (89.4%), over two-thirds (68%) did not know about the counselling remedy.[31] The suicidal ideation in communities flagged by the MSF researchers as a worrying indicator of the level of despair and hopelessness.[32] In areas where MSF operates, community-based mental health care services implemented.[33] In all other Kashmiri districts, community-based mental health services are almost non-existent, despite the intentions set out in the Indian Mental Health Policy to implement such services.[34]

Emergency Health Preparedness in Conflict Situations: The emergency health preparedness in conflict situations is more critical in the realization of the human right to health. The security forces at times obstructed access to urgent medical care for protesters and harassed medical workers and prevented doctors from reaching the hospitals.[35] There were stops by the security forces every 100 to 200 meters to access to the hospital for trauma prevention.[36] Impositions of days-long curfews and police presence in hospitals impeded access to medical care and innovation technologies for the patients.[37] The hospital staff are from far off areas, particularly from south Kashmir is not able to report for work, as strict restrictions placed there.[38]

The Doctors Association of Kashmir said that police had fired tear gas canisters around hospital premises at SMHS and some district hospitals and took videos of the injured and family members accompanying them inside and outside of the hospital emergency room.[39] In situations of unrest and violence, authorities obligated to ensure access to emergency health care as well as to refrain from interfering with health care workers' ability to provide care for all.[40] The right to health in both peacetime and in times of armed conflict or internal unrest ensure equitable access to the highest attainable standard of care without discrimination based on socio-economic status, geographic location, ethnicity, or any other factor.

Conclusion

The violations of human right and humanitarian law in conflicts situations are stupendous in defending the freedom of civilians and combatants to receive medical care. The protection of health professionals who are victims of human rights abuses and to prevent physician complicity in torture and other human rights abuses is also paradoxical to the health delivery system. The hope for peace

and security has engulfed in Kashmiri people collective memory and often seems elusive. The health outcomes of these injuries are amputations, permanent disability or loss of life. The human rights to health and equity in Union Territory of Jammu & Kashmir calls for a robust mechanism of right based approach under humanitarian laws. The central and JK government should immediately stop the use of pellet-firing shotguns and ensure that the use of all other weapons is in line with international human rights standards on the use of force. The authorities should also provide full reparation in line with international standards to those injured by pellet-firing shotguns and to the families of those killed. The doctors from across India asked the government to ease restrictions on communication and travel failing, which is nothing short of a denial of the right to health care and the right to life.

Ethical Clearance: Not Required

Source of Funding: No

Conflict of Interest: No

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Original Article

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An Autopsy Study of Heart in Sudden Death Cases By Triphenyl Tetrazolium Chloride – At Tertiary Care Hospital

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Abstract

Myocardial infarction is the most common cause of sudden unexpected death.On autopsy the evidence of coronary artery narrowing and gross changes are important for the diagnosis. But gross changes took 24 to 48 hours to occur , So the histochemical staining on gross by TTC is more helpful, as it diagnose infarction within 6 hours of death , And also the area from which the section should be taken also can be decided.

Key Words: Myocardial infarction; TTC stain; Gross Diagnosis.

Introduction

Establishment of clinical diagnosis in cases of sudden death due to myocardial infarction is usually difficult and post mortem examination remains the final step in confirming the diagnosis.

The Features characteristic of infarction on H & E stained sections on microscopy are eosinophilia,, swelling of muscle fibers, granularity of cytoplasm, blurring of cell membranes, corrugation of dead muscle fibers, increase in interstitial cells which occurs about 18 hours after death.[1,2]

The changes of identification also shows personal variation, where changes are less. The time required for diagnosis also increases due to the processing time. Actual site of infarction may get missed during sectioning, So the histochemical methods are used that are most sensitive and specific which can detect ischemic areas within 6 hours of death and also differentiate between normal and ischemic area of heart. The actual site for sectioning of heart of infarction area may be missed in the absence of gross localizing techniques.[1,2,3]

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Materials and Methods

The present study is carried out in the department of pathology Dr SCGMC Nanded, from the period of Jan 2019 to Dec 2019.

The heart was examined for the gross, before and after, TTC staining and simultaneously H&E section studied from that area.

Objective

1. To detect myocardial infarction by histochemical staining.
2. To compare the results with H & E stain with histology section.

Inclusion Criteria

Cases of sudden natural deaths suspected of cardiac origin.

Exclusion Criteria

Accidental deaths and deaths due to known cause.

Materials and Methods

The study is carried out on 33 cases of sudden and suspected deaths of myocardial infarction. Proper gross examination with inspection of all valve, aorta and coronaries done. Atherosclerotic changes of coronaries and aorta noted, and also ventricular wall thickness noted. During the medicolegal autopsy the heart is dissected out from the body

thoroughly washed under running water. After weighing, inspection of heart for any abnormalities and malformation done.

The valves are checked for stenosis after opening the atrium. Coronaries are inspected. Myocardium is examined for the gross changes of infarction like softening, hyperemia and white patches.

TTC Test

The heart is sliced from the apex to the atrioventricular junction of 1 to 1.5 cm thick. The slices are incubated in 1% solution of 2,3,5 triphenyl tetrazolium chloride for 20 to 30 mins. The slice should be cleaned in running tap water before incubating to remove excess of blood. The stain is prepared by dissolving 1 gm of TTC powder to 100 ml of phosphate buffer at pH 8.5.

A wide mouth container with screw cap is used to carry out the staining. We used acrylic jar for holding and staining during incubation process it should be screw cap and kept in dark place. As exposure to light and air will make the stain less potent.

TTC solution should be prepared freshly every time and used within half an hour. The slices should be 2 cm beneath the upper fluid level.The pH should be maintained at 8.5 otherwise the formazon pigment formation will be unsatisfactory.

The slices should be turned once or twice during the process for the better results. At the end of staining the slices are transferred to a jar containing 10% formal saline. This halts the reaction also and fix the tissue.

On completion of staining the infarcted part will show pale pink colored area and normal myocardium which takes brick red colour. Even old infarcts, scars can be identified. This staining method is recommended by knight B and LieJT et al.[4]

Results

Total 33 cases of sudden deaths were studied for myocardial infarction. Out of this 30 (90.90%) were males and 3 females(9.09%). The age range between 20 to 80 years.

TTC stain was positive in 26 cases with acute MI, one case with transmural infarct with hemopericardium, (i.e. total 27 cases positive for TTC & out of those 24 cases were positive for histopathological examination as shown in Table 2) three cases which were positive by TTC and not showing changes on histopathological examination, this may be due to early diagnosis by TTC stain and 6 cases have not shown staining by TTC and histopathological examination due to autopsy done within one to two hours of death.

All unstained areas were again studied by histopathological examination, which shows histological changes of MI. The coronaries are also studied with aorta, showed atherosclerotic changes giving support to the diagnosis.

Out of 27 positive TTC cases 24 cases showed microscopic changes of infarction. Six cases of negative TTC do not show microscopic changes. Male cases were more as compared to females and is depicted in Table 1.

Fig. 1A **Fig. 1B**

Fig. 1: A & 1B: Gross Sections of heart specimen before & after staining with TTC dye. Figure 1A Sections of heart before staining with TTC dye Arrow Show's infarcted Area. Figure 1B Sections of heart after staining with TTC dye Arrow Show's infarcted unstained area.

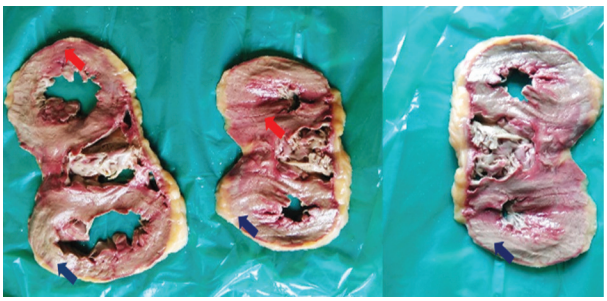

Fig. 2: Gross changes in heart after staining with TTC dye: Red Arrow Shows Normal Myocardial Area Blue Arrow Shows Infarcted Area.

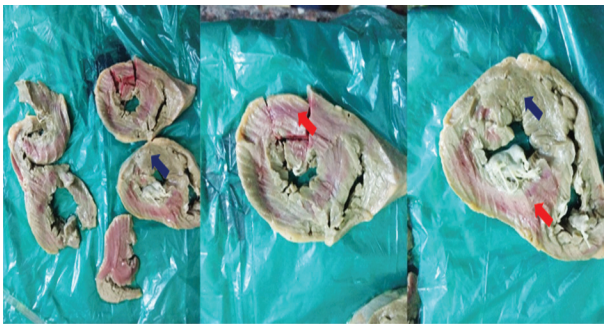

Fig. 3: Gross changes in heart after staining with TTC dye. Red Arrow Shows Normal Myocardial Area Blue Arrow Shows Infarcted Area.

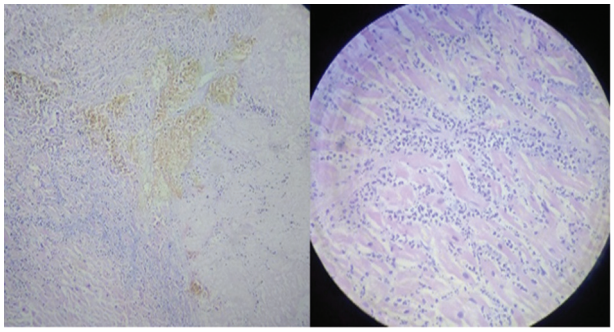

Fig. 4A Fig. 4B

Fig. 4A & 4B : H & E stained section of infarcted area. Figure 4A : Low Power (10x) View Shows Areas of Hemorrahges, Necrosis, inflammation. Figure 4 B: High Power (40x) View Shows hypertrophy Necrosis of myocardial fibers with acute inflammatory cells.

Table 1: Age and Gender Wise Distribution of Cases Included in Study:

Age in Years	Males	Females
Upto 20	-	-
20 To 40	6	1
40 To 60	20	-
60 To 80	4	2
Total	30 (90.90%)	3 (9.09%)

Table 2: TTC and Histopathologicaly Confirmed Cases.

	TTC	Histopathology	Both
Positive	27	24	24
Negative	6	6	6

Discussion

This study is carried on the basis to set the staining method of TTC by pathologist as they have to give final impression of the diagnosis. So in suspected sudden death cases this gross method of diagnosis is really very helpful. This helps to diagnose the infarction of heart.

Diagnosis at autopsy of patients with myocardial infarction occurring within hours of death is often difficult when time lag between irreversible ischemic insult in the myocardium is insufficient for the development of gross and histological changes, indicative of necrosis is less than 6 hours[5,6]. These changes occur between 0 to 12 hours of ischemia.

TTC is salt, which is water soluble and by reaction with normal tissue enzymes forms the light sensitive compound (formazon) which turns normal tissue purple red and abnormal unstained.

There are many biochemical changes in a normal tissue after injury. Similarly the myocardial injury causes leakage of electrolytes like potassium, magnesium, phosphate etc. and various enzymes like lactic dehydrogenase(LDH) Maleic dehydrogenase(MDH), Succinic Dehydrogenase (SDH).

So the histological changes may or may not be there and atherosclerotic changes may or may not be seen. The diagnosis can be given on macroscopic staining method.

The TTC reaction depends upon the activity of these lactic dehydrogenase(LDH) Maleic dehydrogenase(MDH), Succinic Dehydrogenase (SDH) enzymes The inactivation of dehydrogenase enzymes due to leakage out of cell or exhaustion of glycogen stores from within the dead cells, leads to non deposition of formazan pigment over infarcted area.

Inactivation of these enzymes is time bound but variable. It can be noticed as early as five hours of infarction[7]. The enzyme activity can't be affected up to 36 hours and if refrigerated up to 60 hours.[8]

Conclusion

The forensic pathologist has the task of diagnosing Acute MI many times. So before histological changes do appear the pathologist can diagnose the Acute MI by TTC method. This will help in giving the cause of death as well as for benefits of any health policy claim of the diseased.

So routine set up for sudden death cases of infarction TTC is more useful and easy technique, not requiring any costly equipment and can be performed in any set up.

Even 36 hours after death, diagnosis can be given by this TTC method.

So every cases of sudden death and suspected of MI should have this staining strategy to confirm the diagnosis of MI and localizing the area of infarction and the section from the area not stained by TTC can give more positive results by H & E stain.

As our study comprises less samples, more and more studies need to be conducted to establish the definitive data regarding the utility of TTC.

There is no Conflicts of Interest

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Healthcare Ethics and Promotional Advertising: A Difficult Relationship

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Abstract

Participation of health-care professionals in the advertising business has been subject to a raging debate since days beyond recall. It has gained more acceptance but was despised in the past. The Code of Ethics of many National Medical Councils around the world has maintained that for a medical professional to engage in commercial advertising of himself or some other product is unethical-owing to the influence and the cultural authority that a health-care professional holds. This paper reviews instances where medical professionals and bodies have been reported to have explicitly or tacitly lent their support to brand endorsements. Malpractices within the advertising industry in relation to medical fraternity-such as untrue/conjectural claims, distortion of words of a reliable medical body etcetera have also been discussed.

Keywords: Advertising; claims; Distortion; Endorsements; ethics; zohnerism.

Introduction

Being an advertiser/endorser in such a big consumer oriented economy is an attraction strong enough to encourage people to circumvent the attendant rules, regulations and ethics. Due to heavy competition, advertisements have become imperative for brands to secure market shares. There is a cut throat battle for consumer satisfaction and for reaching out to the masses.

One of the most successful advertising strategies includes hiring an endorser that the public trusts. Various sub-populations come under this niche; the public trusts.

Celebrities

Celebrities are loved and idolized in every corner of the world. People place celebrities at proverbial pedestals and by virtue of their acceptance by the masses, celebrities have a huge influence upon even the most aware of all. They hold the power to convince, condition and coerce even the brightest of minds. People want to be them, live their lives vicariously through them, do the things that these influencers do, and by extension, end up patronizing the brands that celebrities may or may not use, but endorse.

The Common People

Apart from the high end denizens of the glamour world, the public trusts the people who they relate to the most. This is by virtue of them having similar needs and a similar pocket size. These type of endorsers will have a typical "neighbor"-like image and the common public tends to go for the products that they have seen their friends, neighbors and people of the same strata use. The viewers feel that if people like them feel satisfied by the product, they would too. Unlike celebrity endorsements-which may leave a scope for disappointment on actual product use.

Medical Experts

Aside from the two subpopulations at the total

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extremes of a spectrum (that have been discussed above), the most trusted source for most people is a medical opinion. Doctors/medical professionals are, in a sense, "local celebrities" to most people. They hold a position of high regard by virtue of their academic knowledge and social status. Doctors are not very commonly associated with the money-making industry, hence whatever they endorse, is taken to be genuine advice by the masses, rather than a money making stunt.

In this research paper, we will focus on the last subset of the population of endorsers usually preferred by advertising companies, and the ethical and legal consequences of the same- as laid out by the MCI in its 'code of ethics'.[1]

Legal history

It is important to understand the legal nuances and the history of it in the field of advertising- especially where it concerns medical professionals. For a long time, endorsements by medical professionals were considered to be unethical as well as unprofessional.

In the U.S, it was not until 1977[2] that the gates of this industry were opened to the healthcare professionals. Before that, advertisements by doctors were looked down upon and considered to be rather distasteful. In 1977, the U.S Supreme Court decision on Bates vs the State of Arizona[2] created a milestone. This permitted attorneys to advertise their services-which they were prohibited from doing previously. Shortly afterwards, the same path was paved for the medical field as well.

Early on, in 1957, The American Medical Association-via its 'Principle of Medical Ethics' maintained-"Solicitation of patients, directly or indirectly, by a physician, by groups of physicians, or by institutions or organizations is unethical. This principle protects the public from the advertiser and salesman of medical care by establishing an easily discernible and generally recognized distinction between him and the ethical physician. Among unethical practices are included the not always obvious devices of furnishing or inspiring newspaper or magazine comments concerning cases in which the physician or group or institution has been, or is concerned.

Self-laudations defy the traditions and lower the moral standard of the medical profession; they are an infraction of good taste and are disapproved"[3] and later in 1984, revised guidelines were published that declared that advertising was an acceptable marketing strategy as long as the claims made were authentic and verifiable. Comparative ads soon became permissible.[3]

Nevertheless, there have still been reservations with respect to advertisements by medical associations, doctors and dentists. Apparently, it is a concept easily embraced by the upcoming generations of doctors while the older, established ones-the veterans-still seem to be finding it rather objectionable.

Discussion

Within the boundaries of the code of ethics laid down by the MCI-the legislative body responsible for the control and governance of all medical education in the country-a doctor can not advertise or solicit his own practice and/or achievements and neither can he advertise any commercial product.[1]

The exact clause states;". Soliciting of patients directly or indirectly, by a physician, by a group of physicians or by institutions or organizations is unethical. A physician shall not make use of him/her (or his/her name) as subject of any form or manner of advertising or publicity through any mode either alone or in conjunction with others which is of such a character as to invite attention to him or to his professional position, skill, qualification, achievements, attainments, specialties, appointments, associations, affiliations or honours and/or of such character as would ordinarily result in his self aggrandizement.

A physician shall not give to any person, whether for compensation or otherwise, any approval, recommendation, endorsement, certificate, report or statement with respect of any drug, medicine, nostrum remedy, surgical, or therapeutic article, apparatus or appliance or any commercial product or article with respect of any property, quality or use thereof or any test, demonstration or trial thereof, for use in connection with his name, signature, or photograph in any form or manner of advertising through any mode nor shall he boast of cases, operations, cures or remedies or permit the publication of report thereof through any mode."[1]

A doctor is, however permitted to use his/her own name/signature where it concerns public health-such as sanitation and hygiene related matters.[1]

All other forms of endorsements are deemed unethical. Hence, doctors are not supposed to participate in advertising cosmetics and/or other 'fast moving consumer goods'

As a medical professional of premium academic knowledge, doctors are free to comment on, say Aspirin as a drug (of-course with necessary

grounds/facts/figures) but not on any particular brand of Aspirin.

This is so because they hold the position of dignity and respect in the eyes of the public hence, whatever they use or recommend is supposed to deeply impact a large population. Medics earn such a position of repute; of-course by virtue of their own hard work but also via the infra-structure and other resources funded out of public money. This increases their responsibility and accountability towards the public by several folds. Accordingly, the 'White Coat' needs to be projected as a symbol of protecting public interest and not at all as that of exploitation for any kind of commercial gains. It is condemnable if any advertising company uses white coat professionals to capitalize on the consumer's lack of knowledge or the faith posed in the goodwill of the White Coat.

Some other problematic practices designed to increase market shares, adopted by corporate sharks (and advertising agencies) include making ambiguous and false claims-such as unsubstantiated 'medical facts', dishing out promotional claims under the garb of 'medical opinions' or declaring something to be "recommended" by a majority of "doctors" and so on and so forth. Such testimonials are more often than not likely to be doctored by picking and choosing of particular phrases-sans prefixes and suffixes-from the original statement by the issuer, wherein disclaimers may have levied heavy conditions on the veracity of the claims made.

Making claims of such nature, or distortion of wordings from an original statement to suit one's own purposes-is not only unethical but may also be deemed as fraudulent.

Among these practices is one popularly referred to as "Zohnerism"[4]. Zohnerism means "the use of a true fact to lead a scientifically and mathematically ignorant population to a false conclusion". This term came into use after a 14-year old Nathan Zohner managed to convince 43 out of 50 people[4] that the chemical-DHMO (Dihydrogen Monoxide) should be banned. He provided logical arguments in his paper as to how it is corrosive in gaseous form, rusts metal and so on. Only a few people were able to catch on the fact that DHMO is essentially water.

Nathan did this project not with the intent of actually getting this 'harmful chemical' banned but to see how gullible the population can be. This practice is rather common in the advertising business-and sometimes in politics as well.

Let us look at a few popular cases and highlight the role of the Advertising Standards Council of India (ASCI) in handling some such violations-some via direct complaints and some suo moto.

1. *Zydus Wellness Ltd (Nycil):* When translated, the advertisement claimed "Not just any other powder, you need Nycil to kill all the germs instantly. Shows results just within three days." This was found to be misleading. Moreover, when viewed in its entirety, the advertisement was observed to be leading its audience to believe that the product is recognized and recommended by doctors for its effectiveness. In light of the Medical Code of Ethics that embargoes advertisements by medical professionals, and in the absence of satisfactory market research data indicating that medical professionals actually recommend the use of the product, the advertisement was found to be ambiguous and misleading.[5]
2. *Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute:* In an advertisement (print), it was claimed; "Pioneers in overcoming Parkinsons" but this claim was not verified or supported by any statistical evidence.[5]
3. A commercial for a renowned pain relief gel claimed "#1 Doctor recommended active for acute pain relief" but the wordings were later found evasive, especially with reference to the terminology "#1 Doctor recommended active" The advertisement lacked a key word "ingredient" which would have made sense to general consumers.[6]
4. *Asian Paints:* In the advertisement for Asian Paints featuring celebrities Deepika Padukone and Ranbir Kapoor, several inaccurate claims were made, such as "Its anti-bacterial technology kills bacteria that enter the house", "Kills all bacteria" "Asian Paints – The Anti-Bacterial Paint. Recommended by the Indian Medical Association". This was later found to be deceptive as the IMA had only permitted the use of their logo for a specific technology namely the "Asian paints silver ion technology" rather than the whole product and had not "recommended" the product. Further probing revealed that the celebrity endorsers had been negligent in checking for the authenticity of the claims with respect to the nature of germ kill action and the time of contact required.[7]

Some more such advertisements that have made unsubstantiated claims from the health-care community include certain Fertility Clinics, notably-Dr. Kavitha IVF Centre, Mothers Lap IVF Centre, GBR Fertility Centres and Hospitals etcetera.[8]

Furthermore, there are abundant instances of erroneous claims made by advertisements regarding Covid-19. Multani Pharmaceuticals Ltd.'s Kuka Cough Syrup can purportedly "stop corona", Alchem Pharmaceuticals' PhytoRelief-CC can "kill the virus in your mouth" and so on[9]. This may also be in violation with the "Drugs and Magic Remedies (Objectional Advertisements) Act" of 1954, section 3(d) which states "no person shall take part in the publication of any advertisement referring to any drug in terms which suggest or are calculated to lead to the use of that drug for the diagnosis, cure, mitigation, treatment or prevention of any disease, disorder or condition specified in the Schedule, or any other disease, disorder or condition (by whatsoever name called) which maybe specified in the rules made under this Act."[10]

To put things into perspective, the ASCI upheld 221 complaints against advertisements in May 2020, 162 of which were related to healthcare.[11]

A significant quantum of such instances sans ASCI involvement include commercial advertisements done by the Indian Medical Association (IMA). A variety of commercial products have been approved and endorsed by the IMA and other such scientific organizations over the years-including Eureka products and Lifebuoy soap.[12] According to a report, the deal between the two parties was worth INR 30 million.[12] Similarly, endorsement of the Tropicana juice brand has reported to have generated INR 5 million.[12] Currently, the agency is understood to be in negotiations with Dabur.[12] The agency maintains that the money earned by such type of endorsements/advertising will be used for seminars, scientific research and conferences.[13]

In 2008, Dr. KV Babu[14], a whistleblower and an IMA Committee Member complained to the MCI about the endorsement of Pepsico by advertising Tropicana and also by use of the IMA logo on Quaker oats cereal claiming that it is in violation with the code of ethics. It was reported to be a contract involving INR 2.25crore.[14] The IMA later argued that it was not endorsing Pepsico, but rather just promoting a 'nutritional program'.

Quite interestingly, the IMA became one of the first such organizations to endorse a food product. Whereas, it is understood to have endorsed several brands such as Lizol, Pampers, Aquaguard, Odomos, Dettol[13] etc.

However, IMA is not the only medical association found to endorse commercial products. Colgate toothpaste and Listerine mouthwash by Pfizer have been endorsed by the Indian Dental Association.[12] It is seen that this practice is rather common on a global scale.

An article by Anupama Sukhlecha[12] reports that in 1988, the American Medical Association had to settle with the Sunbeam Corporation by paying US $9.9 million for their withdrawal from a 5-year endorsement contract. It was regarding the advertisement of medical equipment such as blood pressure monitors and humidifiers.[15] The British Heart Association logo can be seen on Tetley tea[12] and the World Heart Federation logo can be found to have made its way onto the Kellogg's bran flakes packaging.[12]

Another problem is disingenuous advertising which employs medical professional look-alikes (a non-doctor donning a white coat and maybe a stethoscope; referred by the authors of this article as 'White Coat Effect') and advertising some benefits of a product while quoting feedback from clients (and not patients).

While this cleverly exploits the loophole by not engaging a real doctor in the endorsement, it still represents a blatant exploitation of the lack of consumer awareness or, to say the least-unduly cashing from the misuse of the public symbol of medical/health fraternity, whether this un-healthy practice warrants some action by the regulatory bodies is anyone's guess.

A pertinent example of soliciting medical professionals comes from early 20th century- more precisely, from the 1940s. RJ Reynold's Tobacco Company's Camel cigarettes[16] were very popular in a rather competitive niche- thus controlling a market which saw a cut-throat competition. RJ Reynold's claimed "more doctors smoke Camels than any other cigarette"; maintaining that this data was brought forth and verified by "three leading independent research organizations" and asserted to have surveyed 113597 doctors "nationwide" and "from every branch of medicine".[16]

In actuality, the "independent" research organization was RJ Reynold's own advertising service-William Etsy Company.[16] It's employees would conduct their "surveys" in conferences and offices by questioning doctors about their smoking habits and as it later turned out, the subjects of the research were the doctors who were supplied with

complimentary boxes of Camel just prior to the data collection surveys.

All this was happening at a time when no evidenced links were found between cigarettes and the risks they posed to health, but certain inhibitions were emerging regarding the same. This was a new challenge for the tobacco industry; even a potential threat to the otherwise roaring business. While there was a rise in the number of studies that established and affirmed the links between tobacco use and consumer health, the physician-smoker image was reassuring to the consumers, thus ensuring demand and sustaining the business.

Moreover, RJ Reynolds formed a Medical Relations Divisions- the MRD[16]; the sole purpose of which was to work upon attending to researchers willing to reaffirm and reestablish the health claims made by the company.

Afterwards, when speculations arose that cigarette smoke "irritated" the lung tissues, another rookie businessman in the tobacco market- Philip Morris- claimed that his product was "proven" to be "less irritating"- again, a dubious claim at best.[16]

Conclusion

Article 19 of the Indian Constitution protects the citizens' fundamental right of freedom of speech and expression which includes the right to advertise as well. This appears to be going in direct conflict with the medical code of ethics, as per point 6.1, chapter 6 of the Indian Medical Council (Professional Conduct, Ethics and Etiquette) Regulations 2002, which defines advertisement under Unethical Acts.[1] However, it is vital to accord due importance to the MCI Medical code of ethics because the consumers are subjected to a huge amount of ads every day; thereby exposing them to misleading beliefs that a particular brand/product might be of high standards, the medical fraternity is by default associated with, by the public at large. All age groups are profoundly influenced by such commercials but at the same time, children and youth are likely to be more vulnerable, due to their impressionable age.

The viewers are impacted by not only the product that is being advertised but also by the choice of the individual doing it. A responsible advertisement does not promote any sort of negligence and the endorser himself should first verify the authenticity of the claims made by the advertisement, more so by the medical/health professional or anyone who dons a 'White Coat'

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Molecular Fingerprinting a new technique for Personal Identification: An Update

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Abstract

Fingerprints are considered to be most reliable for the personal identification of individuals in criminal investigations, civil disputes and also for routine identification purposes. At different social statuses; there is a need of verification of personality. The most vital and conventional clue in any crime in most circumstances is the fingerprints. Molecular Fingerprints is the new technology in which fingerprint residues contain a large number of inorganic and organic substances in them. Though the inorganic components are present in every fingerprint residue, the presence of those elements/ mineral components may be present in abnormally higher levels indicating / prompting the subject's specific association of them with these elements either due to their occupation, consumption and constant exposure of such elements/minerals or due to the environment with the abundance of such elements in fingerprint residues. This paper reviews many literatures that used only morphometric analysis of the minutiae details or third level details which includes the pore dimensions of fingerprint for Personal Identification. As far as what we found in literature, the study is only limited to Morphometric Analysis. However, based on the literature we reviewed, to filling up the existing research gap, advanced instrumentation techniques were used for the analysis of the elemental composition of the human sweat collected from the fingerprint.

Keywords: Fingerprints; Dermatoglyphics; Molecular Fingerprints; Sweat, Ridge Dimensions; Pore Dimensions; EDXRF; ICP-MS, AFM.

Introduction

Dermatoglyphics is a progressing science and a new method for recording, lifting and developing of prints under different field conditions appearing regularly. Fingerprints are the impressions formed by the ridges of dermal papillae that left on any surface or crime scene when it comes in contact with other surface. It leaves behind sweat traces and other natural secretions from the eccrine glands and some other substances or residue particles that located in the friction ridges of the skin of individual. Several researches were executed on the human population in the field of Dermatoglyphics, which is one of the most accurate projects in the field of forensic technology. Mostly, the fingerprints found at the crime scene are latent prints, which needs to development process either powder or chemical to visualize them. Today, researchers are trying to obtain more information from fingerprints other than loops and whorls, various fingerprint developing methods were used to analyze molecules such as DNA, amino acids, chemicals, drugs or explosives in fingerprint residues.

At different social statuses; there is a need of verification of personality. It is practically compulsory regardless of the activity involved. The detection of crime and criminal identification include different advances and procedures with the available materials. The most vital and conventional clue in any crime in most circumstances is the fingerprints. They are one of the most integral and reliable evidences in any crimes as far as the identification are concerned. To establish the

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absolute identity of the person, fingerprint data base is needed.

The Fingerprint Molecular Identification (FMID) is a new law enforcement technology which will give investigators, prosecutors and government agencies a powerful tool for human identification to build a molecular profile of criminal suspects. By analyzing latent prints residues, Fingerprint Molecular Identification technique can help to reveal not only a gender of the person but also its habits of smoking nicotine or chewing tobacco, medicinal use and illicit drugs, and if a individual had touch a gun or it is exposed to explosives.

Molecular fingerprints are those which contain molecules of those elements which are found in fingerprint as residue. These elements may be abnormally high in their presence in fingerprint. The molecules present in fingerprint residue are generally the excretory products of the physiological functions in the body of human beings. So this will give a probable identity of those substances or minerals which the individual has consumed, ingested, inhaled or exposed to environment by virtue of consumption along with the food due to occupation. Geographical area, habits, occupation, lifestyle, all those factors affect the present of elements in fingerprint residue. For example, specific habits may also be possible to be established with the presence of those molecules indicates habits like narcotine abuse, nicotine habits, chewing tobacco etc.

Due to Occupation -Abnormal quantity of mercury is found in person if he either exposed to environment or ingested mercury or inhalation of Mercury oxide. Abnormal content of copper may indicate the individual lifestyle or occupation. MFID also helps to indicate if a person is exposed to explosive chemicals. Apart from excretory products those contains minerals and abnormal concentration of elements, there are absorbed molecules that indicates the exposure of occupation/habits. Labourers working in Iron / Steel industry, copper utensil industry, casual construction workers may have abnormal content of silica; calcium carbonate indicates the particular environment the individual is exposed to.

Chemical Composition of Fingerprint Residues

The chemical composition of the fingerprint residues altered both quantitatively and qualitatively from the general composition that is the sweat, the major component of fingerprint residue. Sweat contains a different mixture of organic and inorganic compounds coming from the different glands. It has a slightly acidic Ph between 4.0- 6.8 and mean Ph is 6.3. An average of Human body perspire 300–700 mL of sweat in one day .Innumerable contaminants can also be present in sweat consisting of cosmetics, food or drugs and their metabolites.

Secretory Glands

Human skin incorporates 3 types of sweat secretory glands:

Eccrine Gland– Eccrine glands are sweat producing glands and are located throughout the body but the majority are found in the palms of the hands and soles of the feet. The eccrine gland is a tubular shaped structure with a duct that coiled like a helical shape which goes down deep in dermis. Thus play a critical function in fingerprint composition.

Apocrine gland– Apocrine glands are also the sweat producing glands and are large coiled structures which are located near hair follicles primarily in the axillary and perineal regions of the body like arm pits, genital areas etc. Due to their localization, apocrine glands secretion plays a minor role in fingerprint composition but they may be useful in solving sexual offences.

Sebaceous gland- Sebaceous glands that are located throughout the body except for the palms and soles of the feet but the majority of the glands are localised to regions containing hair follicles as well as the face and scalp. The sebaceous glands secrete sebum which is a major component of fingerprint residue.

Eccrine Sweat Composition

Eccrine sweat usually contains excess of 98% water, with innumerable organic and inorganic compounds which varies in quantity in fingerprint residue composition. The rate of eccrine sweat totally depends on the amount of water ingested by a person. Inorganic compounds contain sodium, chloride, calcium, potassium, magnesium, iodide, bromide, sulphate, iron, zinc, phosphate, copper, tin, mercury, lead, manganese, molybdenum, sulphur, cobalt.

Sebaceous Sweat Composition

Squalene, wax esters, triglycerides and phospholipids are the main constituents of sebum produced by sebaceous glands. Other components like glycerides, cholesterol, cholesterol esters and free fatty acids are also present in sebum.

Composition of Eccrine Sweat

Table 1: Major inorganic components present in eccrine sweat residue.

S. No.	Inorganic (major)	Quantity
1.	Sodium	34–266 mEq/L
2.	Potassium	4.9–8.8 mEq/L
3.	Calcium	3.4 mEq/L
4.	Iron	1–70 mg/L
5.	Chloride	0.52–7 mg/mL
6.	Fluoride	0.2–1.18 mg/L
7.	Bromide	0.2–0.5 mg/L
8.	Iodide	5–12 µg/L
9.	Bicarbonate	15–20 mM
10.	Phosphate	10–17 mg/L
11.	Sulphate	7–190 mg/L
12.	Ammonia	0.5–8 mM

Table 2: General organic components present in eccrine sweat residue.

S. No.	Organic (General)	Quantity
1.	Amino acids	0.3–2.59 mg/L
2.	Proteins	15–25 mg/dL
3.	Glucose	0.2–0.5 mg/dL
4.	Lactate	30–40 mM
5.	Urea	10–15 mM
6.	Pyruvate	0.2–1.6 mM
7.	Creatine	
8.	Creatinine	
9.	Glycogen	
10.	Uric acid	
11.	Vitamins	
	Organic (Lipids)	**Quantity**
1.	Fatty acids	0.01–0.1 µg/mL
2.	Sterols	0.01–0.12 µg/mL

Composition of Sebaceous Sweat

Table 3: Major and trace organic components present in sebaceous sweat residue.

S. No.	Organic (major)	Quantity	Organic (trace)
1.	Triglycerides	30–40%	Aldehydes
2.	Free fatty acids	15–25%	Ketones
3.	Saturated	50%	Amines
4.	Monounsaturated	48%	Amides
5.	Polyunsaturated	2%	Alkanes
6.	Wax esters	20–25%	Alkenes
7.	Squalene	10–12%	Alcohols
8.	Cholesterol	1–3%	Phospholipids
9.	Cholesterol esters	2–3%	Pyrroles
			Pyridines

Personal Identification using dermatoglyphics

Many researchers have studied different variables of personal identification using fingerprints. Acree (1999) reported the gender differences in fingerprint using ridge densities among Caucasian and African American population. The study revealed that there is higher fingerprint ridge densities found in females of Caucasian and African American population than males. (MA, 1999). Dr. A. Bharadwaja et. al (2004) studied the dermatoglyphic pattern and blood groups of 300 students of different ABA blood groups of JLN Medical College, Ajmer and total ridge counting(TRC) was done and found that people having blood group A have more loops whereas blood group AB had more whorls. Total fingerprint ridge count (TFRC) is higher in number in blood group B followed by blood group O. (Dr. A.Bharadwaja, March 2004) Sudesh Gungadin (2007) also reported similar observations in Indian population. He has taken 500 subjects (250 males and 250 females) in the age group of 18-60 years from karnataka. (Gungadin, 2007). Jaydip Sen et. al. (2008) compared the palmar dermatoglyphics prints of two ethnic Indian populations of North Bengal i.e Rajbanshi and Mech. They collected 192 prints from the Rajbanshi and 100 prints from Mech population of age group of 18-60 years using roller and ink method. The results showed significant differences between dermatoglyphic variables. (Sen J, 2008)

A recent study also found observations that are reported in Spanish Caucasians Gutierrez-Romero, et al.(2008) tried to prove the gender differences based on fingerprint. The samples were collected from 100 males and 100 females of age ranges between 20-30 years old to determine the ridge density in the Spanish population samples. (Gutierrez-Redomero E, 2008). Vinod C. Nayak et. al (2010) study the sex differences in fingerprint ridge density in Chinese and Malaysian population. They collected 200 prints from Chinese population (100 males and 100 females) and 100 samples from Malaysian population (50 males and 50 females) and found that females have greater ridge density hence, finer ridge details than men in Chinese and Malaysian population there is significant gender differences occur in the finger ridge density. (Nayak VC, 2010)

Dr. Prateek Rastogi and Ms. Keerthi R Pillai (2010) described the relationship between fingerprint patterns, blood group and gender. The study was carried out on 200 students (100 male & 100 female) within the age group 18-25 of Kasturba Medical College, Mangalore. The results obtained

were every fingerprint is unique; Males have significant higher count of whorls while females have a higher count of loops. They have also found that Loops show more predominance in blood group A, B, AB and O in both Rh positive and Rh negative individuals except in O negative where whorls are more common. (Dr. Rastogi Prateek, 2010) Nithin MD et. al (2011) determine the gender based on finger ridge count. They have collect Rolled fingerprints from 550 subjects (275 men and 275 women) belonging to South Indian population of age group of 18-65 years.

The results they have found showed that women have a significantly higher ridge count than men. (Nithin MD, 2011). Monika Bhardwaj et. al (2011) study the differences in the ridge count of loop pattern among 50 male and 50 females belonging to Amritsar city (Punjab) of age group between 18-45 years. From the fingerprint slip, only the loop pattern were selected and ridge count were done and ANOVA analysis were performed which shows that there is no significant difference found in the ridge count of loop pattern among gender. (Monika Bhardwaj, 2011) Ramanjit Kaur et. al (2011) examined the epidermal ridge density of two Northern Indian populations (Sikh Jat and Bania) they have collected 50 samples of each population (25 males and 25 females) aged between 18–50 years from Punjabi University campus, Patiala. The study found that 92% of Sikh Jat females have a mean ridge density above 13, whereas 76% of Sikh Jat males have (a mean ridge density) below 13, while in Bania, 100% of females have mean ridge density above 14 and 80% of males – below 14 which shows there are significant differences in epidermal ridge density between males and females within each of the two populations. (Ramanjit Kaur, 2011)

Murlidhar Reddy Sangam et. al (2011), observed that there were significant sex and bimanual differences in the distribution of the finger print pattern in 268 males and 238 females, of NRI medical college, Chinakakani, Guntur, Andhra Pradesh and also observe the bilateral asymmetry. The results obtained that whorls are present in high frequency on thumb, index and ring fingers in males. But females show higher frequency of loops on all fingers expect ring finger. Also it has been found that whorls are more common in right hands where as arch pattern and radial loops are more on left index finger. (Murlidhar Reddy Sangam, 2011 June) Varun Parmar et. al (2012) establish the correlation between the age and sex of 100 individuals along with the ridge density of the fingerprints among Gujarati Population. And it was found that there is an increase in the ridge width during childhood age (from 6years) to adulthood (upto25 years) and then there is a reduction in the ridge width in middle age and again there is an increase in ridge width with the advancement in age. (Varun Parmar, 2012) Arun Kumar Agnihotri et. al (2012) identify the ridge density and compare it between 200 subjects i.e. (100 men and 100 women) within the age range of 20–30 years in the Indo-Mauritian population . The results they have found that ridge densities in female hands are much higher compared with those in male hands. (Agnihotri AK, 2012) Gagandeep Singh (2012) examined the differences in ridge density of two Northern Indian populations (50 Khatris and 50 Banias within age group 18-40 years of Chandigarh region and found that 92% of Khatri females have a mean ridge density above 13, whereas 76% of Khatri males have a mean ridge density below 13, while in Bania, 100% of females have mean ridge density above 14 and 80% of males below 14. (Singh, 2012)

Kewal Krishan et. al (2012) studied the ridge density variation of 194 individuals (97 males and 97 females) age group ranges from 18-25 years of different schools and colleges of Palampur city, District Kangra Himachal Pardesh and found that females have a higher fingerprint ridge density than males in all the three radial, ulnar and lower areas of the fingerprint pattern. (Kewal Krishan, 2012) Esperanza Gutierrez-Redomero et. al (2013) studied the variation in ridge density in 100 male subjects aged between 18-48 years of Sub-Saharan population and compared the results with the Spanish populations and found that Sub-Saharan male subjects has lower ridge density than Spanish male subjects in the distal areas of all fingers, whereas differences were seen in the proximal region only on some fingers. (Esperanza Gutierrez-Redomero, 2013) Lalit Kumar et. al (2013) studied the correlation between sex and fingerprint ridge density in 250 subjects (125 males and 125 females) of age group 18-60 years of Dehradun (Uttarakhand) and found that women have significantly greater ridge density than men. (Lalit Kumar, 2013) Neeti Kapoor et. al (2014) studied the thumbprint ridge density of 100 males and 100 females of age group 18-30 years in a central Indian (Marathi) population and observed that females have a higher thumbprint ridge density than males. (Neeti Kapoor, 2014) S. F. Abdullah et. al (2015) uses the fingerprint ridge density to classify the gender in population of northern part of Malaysia. The sample of 50 participants i.e. (25 males and 25 females) of age ranges from of 18-60 year. The results obtained shows that women

have a significantly higher ridge count i.e. 15.1 as compared to men i.e. 11.4. (S. F. Abdullah, 2015) Amit Chauhan et. al (2015) studied the ridge density differences by developing the latent prints on the paper of 60 (males and females) within age group 18-55 years of Uttar Pradesh population and found that there is significantly higher ridges densities present in females as compared to males. (Chauhan Amit, 2015)

Pattanawit Soanboon et. al (2015) compare the ridge density of 353 male and female teenagers of Thai population within age group of 18-24 years with an intention to determine the topological, age-grouping and sexual differences in fingerprint ridge density (RD). The results obtained shows that females have a higher ridge density i.e. narrow ridges than males. (P. Soanboon, 2015). Jasmine Kaur Dhall et. al (2016) examined the ridge density of the index finger of right hand of 245 males and 246 females of Punjabi (Arora and Khatri population) within age group of 18-65 years of Delhi region. In a single digit, 5 ridge density count areas were selected and the results obtained shows that females have significantly higher ridge density than males in all the 5 selected areas. (Kapoor, March 2016).

Noemí Rivaldería et.al (2017) studied the fingerprints of the Buenos Aires and Chubut provinces in Argentina to quantifying the variations used for personal identification. Samples were obtained from 330 individuals, (170 Male and 170 Females), from two Argentinean population and minutiae were identified and studied. (N. Rivaldería, 2017) Govindrajulu Rajesh Babu et. al (2018) studies the ridge dimensions of normal people in comparison with the worker class along with the nail clips and hair and obtained significant results which is prospective occupation markers. (Govindrajajulu Rajesh Babu, 2018). Amit patil et.al (2018) determine the fingerprint ridge density of total 170 subjects (70 males and 100 females) within age group of 18-65 years of Dr D Y Patil Medical College and Hospital, Nerul, Navi Mumbai to see the sexual differences in them and confirms that females have higher ridge density than males. (Dr Amit Patil, 2018)

Sampling of Sweat

Sweating is normally exceeds by anxiety, work out, stress and sickness and sometimes also diminished by cold. Sweat secretion sometimes also influenced by different variables like, temperature, humidity, hormonal imbalances, overactive thyroid gland, certain food and prescriptions. For sampling purposes, sweat should be collected in a sufficient volume that would be enough for analysis. Various sweat samplers are introduced now days for collection of sweat. A drug named Pilocarpine is used to stimulate sweating. The basic technique for collection of sweat involved use of Glass micro fibre filter paper of 0.22 micron. The water from the filter paper evaporates leaving concentrated sweat components which will be used for further sweat analysis. To overcome this problem of water evaporation from sweat, eppendorfs with air-tight lids are used to collect minimum 3 (L) of sweat by several times.

Instruments used for sweat Analysis

1. *Energy Dispersive X-Ray Fluorescence Spectrometer (EDXRF):-*X-ray fluorescence (XRF) spectrometry is an elemental analysis technique commonly used for identification and quantification of elements presents in substance. The materials can be solid, liquid, or semi-solid. This technique is rapid, accurate, non-destructive, and sensitive for heavy metal analysis. It requires a minimum of sample preparation. It can detect concentration up to ppm levels. It covers all elements from Sodium (Na) to Uranium (U) levels.
2. *Inductively Coupled Plasma-Mass Spectrometer (ICP-MS):* It is a type of mass spectrometry in which plasma gas to used ionize the sample and detect the elements present in the sample with atomic mass ranges from 6 to 256 (${}_{6}Li^{3}$ to ${}_{256}U^{92}$) both qualitatively and quantitatively. It mainly works with the liquid samples. For solid samples, we need to do the sample preparation by making the sample in liquid form. It can detect the trace elements up to 1 ppq to 100 ppm levels.
3. *Ion Chromatography:* It is a process that separates ion and polar molecules based on their affinity to ion exchange. It works on almost any kind of charged molecule. It is used to measure concentrations of major anions like fluoride, chloride, nitrate, nitrite, and sulphate and major cations like lithium, sodium, ammonium, potassium, calcium, and magnesium up to (ppb) range. It also helps to measure certain charged organic compounds i.e. proteins, amino acids, nucleotides etc.
4. *Atomic Force Microscope (AFM):* An Atomic force microscope is a advanced type of scanning probe microscope that has high resolution and detect in nanometers scale. It records the topographical features of the surface and measures vertical as well as

Table 4: Shows the work done by the authors on different population groups.

S.No	Author's Name	Work	Year	Population Study	Journal
1.	Acree	Gender differences in Ridge Dimensions	1999	Caucasian and African American population	Forensic Science International
2.	Dr. A. Bharadwaja	ABA blood group , TRC, ridge dimensions	2004	Students of Ajmer, Rajasthan	Journal of Forensic medicine & Toxicology
3.	Sudesh Gungadin	Gender differences in Ridge Dimensions	2007	Karnataka Population	Internet Journal of Medical Update
4.	Jaydip Sen	Gender differences in Ridge Dimensions	2008	Rajbanshi and Mech of North Bengal	Journal of Forensic Sciences
5.	Gutierrez-Romero	Gender differences in Ridge Dimensions	2008	Spainish Population	Journal of Forensic Sciences
6.	Vinod C. Nayak	Gender differences in Ridge Dimensions	2010	Malaysia Population	Forensic Science International
7.	Dr. Prateek Rastogi	Relationship between fingerprint patterns, blood group and gender	2010	Students of Mangalore, Karnataka	Journal of Indian Academy of Forensic Medicine
8.	Nitin MD	Gender differences in Ridge Dimensions	2011	South India Population	Journal of Forensic and Legal Medicine
9.	Monika Bharadwaj	Gender differences in Ridge Dimensions	2011	Punjab Population	Journal of Life Sciences
10.	Ramanjeet Kaur	Gender differences in Ridge Dimensions	2011	Sikh Jat and Bania Population	Problems of Forensic Sciences
11.	Murlidhar Reddy Sangam	Gender differences in Ridge Dimensions	2011	Andhra Pradesh Population	Journal of Clinical and Diagnostic Research
12.	Varun Parmar, Rajesh Babu	Age and Gender differences in Ridge Dimensions	2012	Gujarati Population	Journal Of Karnataka Medico Legal Society
13.	Arun Kumar Agnihotri	Gender differences in Ridge Dimensions	2012	Indo-Mauritian Population	Medical, Science and the Law
14.	Gagandeep Singh	Gender differences in Ridge Dimensions	2012	Khatri and Bania Population	Journal of Forensic Research
15.	Kewal Krishan	Gender differences in Ridge Dimensions	2012	Kangra, Himachal Pradesh Population	Journal of Forensic and Legal Medicine
16.	Esperanza Gutierrez-Redomero	Gender differences in Ridge Dimensions	2013	Sub-Saharan and Spanish Population	Forensic Science International
17.	Lalit Kumar	Correlation between sex and fingerprint ridge density	2013	Uttarakhand Population	Journal of Indian Academy of Forensic Medicine
18.	Neeti Kapoor	Thumbprint ridge density	2014	Marathi Population	Egyptian Journal of Forensic Sciences
19.	S.F.Abdullah	Gender differences in Ridge Dimensions	2015	North Malaysian Population	ARPN Journal of Engineering and Applied Sciences
20.	Amit Chauhan	Ridge Density (RD) of the index finger of right hand	2015	Uttar Pradesh Population	Research Journal of Recent Sciences
21.	Pattanawit Soanboon	Topological, age-grouping and sexual differences in fingerprint ridge density	2015	Thai Population	Egyptian Journal of Forensic Sciences
22.	Jasmine Kaur Dhall	Gender differences in Ridge Dimensions	2016	Punjabi Arora and Khatri Population	Journal of Forensic Sciences
23.	Noemi Rivalderia	Minutiae and Ridge Counting	2017	Argentina Population	Science and Justice
24.	Govindrajulu Rajesh Babu	Ridge Dimensions and occupation markers	2018	Construction workers	Voice of Intellectual Man
25.	Amit Patil	Gender differences in Ridge Dimensions	2018	Hospital staff of Navi Mumbai	IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)

Sweat Sample Preparation for Analysis

1. *Energy Dispersive X-Ray Fluorescence Spectrometer (EDXRF):* The sweat samples collected on Glass Micro Fibre Filter Paper and were carefully kept with sterile forceps in the sample holder covered with Mylar sheet and placed in the chamber.
2. *Inductively Coupled Plasma-Mass Spectrometer:* For ICP-MS the sweat samples on Glass Micro Fiber Filter Paper were taken in fresh falcon tubes of 15ml each and were extracted with Aqua Regia which is a solution nitric acid and hydrochloric acid at a ratio of 1: 3. Further filtration was performed after 24 hours and to the filtrate de-ionized water was added to make up till 10ml for the analysis.
3. *Ion Chromatography:* Around 50 mg of the sweat sample is accurately weighed into a clean 10 ml standard flask, the content is diluted and made up to the mark with diluting agent i.e. Ultra Pure water and sonicated for 3 minutes. It is filtered through 0.2 µ filter paper and then injected into the ion chromatograph.
4. *Atomic Force Microscope (AFM):* For Fingerprint sample, no sample preparation is required.

Research Gaps, Limitations and Outcomes

In view of the numerous studies that have been carried out on fingerprints for personal identification, it has been found that the previous researches are only limited to morphometric analysis of the minutiae details or third level details which includes the sweat pores dimensions. With the advancement in the techniques for personal identification, there is a need for better understanding and implementation of new methods which is helpful in the study. The extents of majority of the previously existing studies are restricted to either a single category of ridge density and ridge count.

Hardly, there are handful amount of studies relating to chemical analysis of fingerprint sweat in relation to both ridge and pore morphometric analysis for personal identification. Therefore, for filling the existing research gap, advanced instrumentation techniques were used for the analysis of the elemental composition of the human sweat collected from the fingerprint. Along with that, other than ridge thickness and ridge density measurements, angle variations, total fingerprint ridge count (TFRC), Bilateral Symmetry of the fingerprint pattern can be performed.

Applications of Fingerprint Analysis

1. It helps in individual profiling for identification of the person.
2. It helps to identify the elemental composition of fingerprint residue of people belonging to various geographical areas.
3. It helps to identify the ridge and sweat pore dimensions of the dermatoglyphic pattern of different population.
4. It helps to identify the habits, lifestyle and environment from which the individual is exposed to.
5. It also helps in the diagnosis of diseases like cystic fibrosis, diabetes mellitus etc.

Conclusion

Several researches were performed on the human population in the field of dactylographics; fingerprints are used for personal identification due to their individuality, uniqueness, and permanence. The present study is an attempt to analyse the fingerprint residue for personal identification and with the advancement of the technology, it is necessary to make use of new instrumental techniques for analysis purpose. Based on the fingerprint minutiae morphometric and morphological analysis, it has been found in numerous studies and also it would be universally accepted that women tend to have more ridge density than men. Other than that the main components of fingerprint residue i.e. sweat which is considered as a bio fluid also plays an important role as a prospective marker for personal identification.

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Case Report

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Sirenomelia Apus with Cystic Dysplastic Kidney A Rare Polymalformative Syndrome

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Abstract

Sirenomelia is a lethal form of caudal regression anomaly which shows fusion of the lower limbs with a spectrum of anomalies affecting musculoskeletal, genitourinary and gastrointestinal systems.It resembles a mermaid in Roman mythology, with upper body of a human and the lower half resembling the tail of a fish.We report a case of anomalous fetus diagnosed at 18 weeks of gestation born to a non-diabetic mother.External phenotype showed fused lower limbs, no discernible external genitalia, imperforate anus,hypodactyly, ectopic cystic dysplastic kidneys and Potter's syndrome with single umbilical artery. Maternal diabetes has been associated with caudal regression syndrome and sirenomelia. Here we report a case of Sirenomelia with Potter's syndrome and cystic renal dysplasia not associated with gestational diabetes mellitus. The presence of cystic renal dysplasia in our case would further endorse the mesodermal defect in caudal regression syndrome. The possible use of genetic analysis will help to analyse the underlying molecular mechanisms of caudal regression syndrome associated with cystic renal dysplasia.

Keywords: Sirenomelia; Cystic Renal Dysplasia; Potter' Syndrome; Hypodactyly.

Introduction

Sirenomelia is an extremely rare anomaly with an incidence of 0.8-1 case/100000 births.[1,2,3] It shows fusion of lower extremities with anomalous musculoskeletal, genitourinary and gastrointestinal systems. Sirenomelia is the severe form ofCaudal regression syndrome (CRS)that encompasses a wide spectrum of congenital anomalies resulting from an embryonic defect due to injury to the caudal mesoderm in the early gestation during gastrulation.[4,5] When features of Potter's facies are combined with olighydramnios and pulmonary hypoplasia, it is known as Potter's syndrome.[6]

Sirenomelia has a strong association with maternal diabetes and 10-15% of fetuses with this anomaly have been born to diabetic mothers.[1,7] Renal Cystic Dysplasia (RCD) has been reported to be associated with caudal regression syndrome.[5]

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Case Report

A 22 year old primigravida on antenatal ultrasonography scan was detected to have anomalous fetus with lower limb deformity, absent kidneys and anhydramnios at 18 weeks of gestation. The pregnancy was terminated and the fetus weighed 340 grams.

External examination showed fused lower limbs, bilateral absent feet, no discernible external genitalia, imperforate anus, left upper limb hypodactyly and Potter's facies (large low-set ears, prominent epicanthic folds, hypertelorism, flat nose and receding chin)(Fig.1). Internal examination showed left lung hypoplasia, absent kidneys in lumbar area, ectopic cystic kidney in pelvic cavity attached to mesentry and a single umbilical artery(Fig. 2).

Fig. 1: External anomalies: Fused lower limbs, Left upper limb hypodactyly (4 fingers)- Absent thumb, imperforate anus, indiscernible external genitalia and Potter' facies(large low-set ears, prominent epicanthic folds, hypertelorism, flat nose and receding chin)

Fig. 2: Cut section of umbilical cord showing a single umbilical artery and a vein.

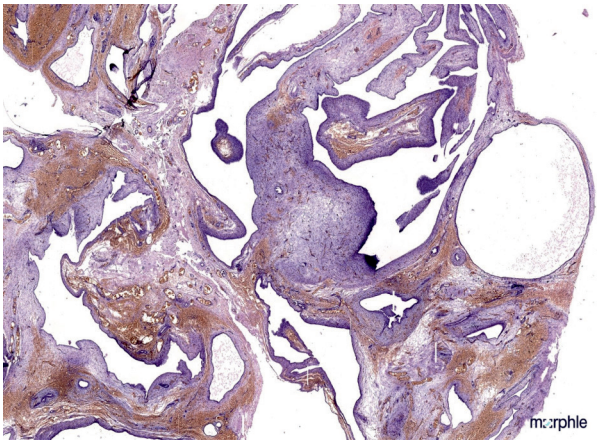

Fig. 3: Cystic dysplastic kidneys displaying multiple cystic spaces lined by flattened cuboidal epithelium.

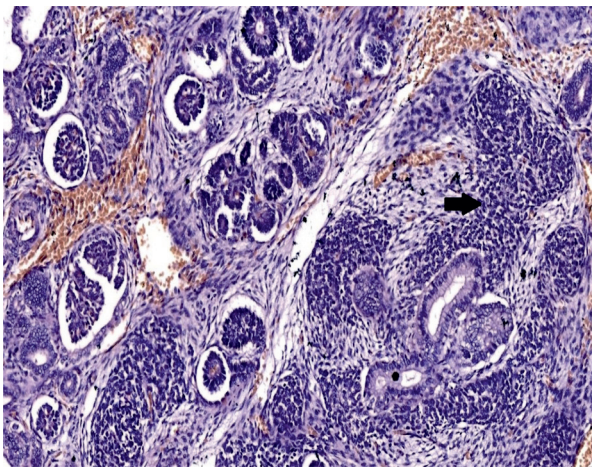

Fig. 4: Foci of nodular blastema -undifferentiated cells (arrow) and primitive glomeruli.

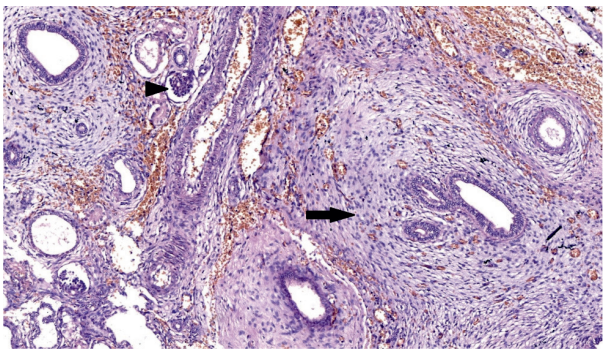

Fig. 5: Islands of undifferentiated mesenchyme, immature collecting ducts with fibromuscular collars (arrow) and primitive glomerular structures (arrowhead).

Microscopic examination of the cystic mass showed renal glomeruli embedded in a stroma consisting of multiple cystic spaces lined by flattened epithelium(Fig.3). Foci of nodular blastema composed of undifferentiated cells were seen(Fig 4). Immature collecting ducts with fibromuscular

collarsand primitive glomerular structures(Fig 5) werediagnostic of cystic renal dysplasia-Potter Type 2. A diagnosis of SirenomaliaApus with Potter's syndrome, hypodactyly and renal cystic dysplasia was made.

Discussion

Caudal regression syndrome (CRS) encompasses a wide spectrum of fetal anomalies with varied degrees of severity. The most severe extreme end of the spectrum is fusion of the lower limbs with major organ malformations, known as sirenomelia, while the mildest form is imperforate anus.[5] Sirenomelia is associated with visceral abnormalities encompassing lumbosacral and pelvic malformations, such as sacral agenesis, malformed vertebrae and hemivertebrae, absent or malformed external and internal genitalia, imperforate anus, cleft palate, pulmonary hypoplasia, and cardiac defects.[7] Sirenomelia is incompatible with life with more than half the cases resulting in stillbirth and those born alive die within a day or two of birth because of severe visceral anomalies involving abnormal kidney and bladder development.[6,7]

In 1987, the theory of vitelline artery steal was hypothesised by Stocker and Heifetz and reported that consistently all patients with sirenomelia had a large umbilical artery derived from a persistent vitelline artery. Thevitelline artery reduces the bloodflow and feeds the caudal portion of the embryo by diverting bloodflow from the embryo to the placenta. Theremaining branches of the aortic arteries are either absent or hypoplastic.[2,3] The end result is sacral hypoplasia, renal agenesis, bladder and ureteral hypoplasia, deficiency of the genitalia, and malformations of lowerlimbs. The second hypothesised theory is of defective blastogenesiswith hypoperfusion, leading to insufficient growth and incomplete development of the caudal region.[3]

Sirenomelia has been hypothesized to be caused by sporadic mutation and thought to be the result of combined genetic and environmental components.[5,7] Though genetic defects in humans are still unknown in the mermaid syndrome, two defective genes Cyp26a1 and BMP7(bone morphogenic protein) genes have been identified in mice for the birth of a mermaid neonate.[3]

The environmental risk factors described for caudal regression anomalies are multiple such as retinoic acid, maternal diabetes and heavy metals.[7] Mothers younger than 20 years and older than 40 years are known to be vulnerable.[1] Gestational diabetes mellitus has been implicated in 10–15% of affected fetuses.[1,3,7] An association with drug abuse such as cocaine, has also been described in the causation off sirenomelia in a few reported cases.[1,7] The present case showed no association with maternal diabetes or drug abuse which can be an additional plea to other environmental causes and genetic causes which need further study.

Stocker and Heifetz classified sirenomelia into seven types Type I to type VII, based on the presence of skeletal elements inlower limb. In type I, the mildest form, the fusion only affects superficial tissues with all bones in the two fused limbs being present. In type VII, the most severe form, only a single lower limb bone is present, with no indication of legs or feet.Sirenomelia used to be classified as sympusdipus or symmeliawhen two feet were present, sympusmonopus or uromelia when only one foot was discernible, and sympusapus or sirenomeliaapuswith no evidence of distal foot.8In our case, based on external examination finding of absent feet, it is classified as SirenomeliaApus.

Potter syndrome and Potter facies, a facial abnormality has been described to be frequently asssociated with cases of sirenomelia, as in our case. Potter's syndrome is a triad of Potter'sfacies (large, low-set ears, prominent epicanthal folds, flat nose, hypertelorism, and receding chin), oligohydramnios and pulmonary hypoplasia. This syndrome is almost invariably associated with bilateral renal agenesis.[1,6]

Our case had hypodactyly with absent thumb and hypoplastic thumb has been previously reported to be associated with sirenomelia.3,6Single umbilical artery has been associated in 100% cases ofsirenomelia as in our case.[9]

Renal Cystic Dysplasia (RCD) has been documented to be associated with caudal regression syndrome.[5,10] In a fetopathologic study of 74 cases of renal cystic diseases, RCD was isolated in 19% cases, associated with obstructive uropathy in 12% cases and polymalformative syndrome in 69% cases. Among the unclassified polymalformative syndromes, the renal dysplasia was part of caudal regression syndrome (CRS) in 6/18 of fetuses.[5]As the kidneys and ureters are developed from the mesoderm, it can be hypothesised that, the presence of cystic renal dysplasia in cases of sirenomelia would affirm the mesodermal defect in caudal regression syndrome as in our case.[10]

Renal cystic disease in the present fetus was type 2 according to potter classification:

type 1;Infantile polycystic kidney disease

(ARPKD Autosomal recessive polycystic kidney disease), type 2;cystic dysplastic kidney [MCDK-multicystic dysplastic kidney disease]), type 3; adult polycystic kidney disease (ADPKD); and type 4; urinary outflow obstruction (obstructive dysplasia).[11] Renal dysplasia is diagnosed by primitive ducts with a fibromuscular collar and lobar disorganization. The other microscopic findings include metaplastic cartilage, bone, nodular renal blastema, and proliferating nerves.[12]

Caudal regression syndromes with multicysticrenal dysplasia are frequently sporadic. A pilot study by Porsch et al.has recently identified three candidate genes, the known tumor suppressors, PDZD2, GLTSCR2 and PTEN by whole exome sequencing and copy number variation analyses. These have been previously identified in a patient affected with VACTERL: association of vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities. This study makes it imperative to screen these candidate genes in multicystic renal dysplasia associated with CRS.The current use of whole exome sequencing may help to elucidate the underlying molecular mechanisms of cystic renal dysplasia of unknown etiology associated with caudal regression syndrome.[10]

Conclusion

Antenatal ultrasonography as early as 13-15 weeks of pregnancy can detect gross fetal structural anomalies associated with caudal regression syndrome. Early diagnosis is imperative for immediate termination of pregnancy that can be safely advised to the mother to prevent maternal morbidity and mortality. Further molecular and genetic studies are warranted for the identification of possible candidate genes in a polymalformative syndrome.

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Article in supplement or special issue

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[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www.statistics.gov.uk/downloads/theme_health/HSQ20.pdf (accessed Jan 24, 2005): 7-18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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