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EDITORIAL

SECOND WAVE OF COVID-19 IN PAKISTAN; HOW WORSE IT CAN GET?

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The outbreak of Corona Virus which was initiated as Pneumonia of unknown origin in December 2019 in Wuhan, China was declared by WHO as the sixth Public Health Emergency of International Concern (PHEIC) on 30th January 2020 and officially the name given to this illness was Corona Virus Disease-19 (COVID-19). The first case of coronavirus was reported in Karachi, Pakistan on 26th February 2020.

In the first wave of COVID-19, when the number of cases was rapidly increasing, the Government of Pakistan imposed a strict lockdown restraining the public transport, markets, hotels/restaurants, shopping malls, marriage halls, educational institutions, and recreational sports, etc. Then, due to severe threats to the national and individual economic status, the lockdown was modified to a "smart" lockdown to focus only on the "worst-hit: areas. In this way, Pakistan handled this Pandemic reasonably and this policy was very well endorsed by the international observers. The National Coordination Committee (NCC) declared the Pandemic under control in its meeting on 7th August 2020. On 5th September 2020, no new case of the corona was reported and the death rate was reduced to 3 per day only. However, that mislead people and they started their routine work all around the country.[1]

Although the Government of Pakistan continued warning the people of Pakistan to continue observing the precautionary SOPs, but the people were so much relaxed that they started their routine activities, as usual, all over the country. The opening of shopping malls, hotels/restaurants, marriage halls, educational institutions, and recreational spots, etc. resulted to increase again in the number of corona cases every day.

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People started neglecting all the SOPs. Initially, the Government of Pakistan did not take any strict action considering again the economic status of the country but that policy failed to control the spread of the second wave of the corona. Slack and inefficient policy and lockdown gamble paved the way for Covid-19 spread through political, religious, social, regular business activities, tourism, and transport. Not just that, the colleges, schools, and universities were also re-opened for regular activities across the country.

Ease in lockdown, with the opening of shopping malls and all areas of public gatherings, resulted in havoc and increase in the cases every day, people also started attending weddings and gatherings and were barely following SOPs. The government and authorities were well aware of the situation but ignored the option of lockdown considering that it would ruin the country's economy and thus have failed to control the spread of pandemic due to non-implementation of strict rules and fines to the locals.[2]

Things got out of hand when the lockdown was uplifted which eventually led us to the second wave of the pandemic. It is highly foreseeable that Covid-19 can become a source of persistent infection if such non-serious attitude of the people and ignorance by authorities continues.[3] With a spike in everyday cases, the government officially announced the second wave of Covid-19 in Pakistan on 24 October 2020 which resulted in > 3000 new cases, just like back in July when the first highest number of cases were reported. Health experts say that the second coronavirus wave could prove to be more fatal than the first wave in the country[4] which claimed 332,186 infected, 6795 lives, left behind 632 on ventilators.[2] Until November 24, 2020, there were 2954 confirmed cases

and 48 deaths in a day which is highly alarming[5], after which the authorities announced a smart lockdown from November 26, 2020, as a measure to stop the spread of coronavirus. Other notifications were also released including; closure of educational institutions, ban on indoor events and ceremonies in marriage halls[6] public and private sectors were directed to ensure that 50% of the staff works from home till January 31 2020.[7]

On December 13, 2020, the cases were 2,456 with 36 deaths in 24 hours.[8] (Figure-1) Although, now again the number of new cases is gradually reducing but still until 31st December 2020 there were 2463 new cases and 71 deaths in a day is still very alarming. We are very far from the flattening of the curve (Figure-2). Spiking infection rates could swamp the inadequate health system and cripple the economy of the country. If citizens are not provided with proper care or adequate aid as the economy shrinks, public anger is likely to elevate, potentially threatening the social order. We have to be more serious and cautious while playing our roles at the individual level to control the spread of the disease before it's too late and the irreparable damage is done to the economy and community as a whole.

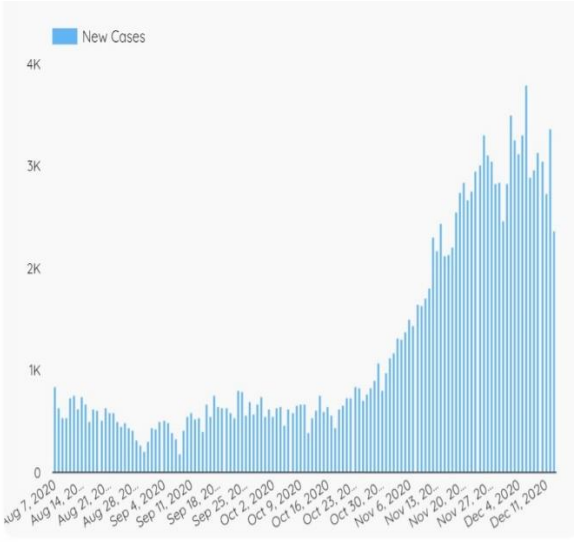

Figure-1: Daily Covid-19 Cases in Pakistan till the first week of December 2020. (https://covid.gov.pk/stats/pakistan)

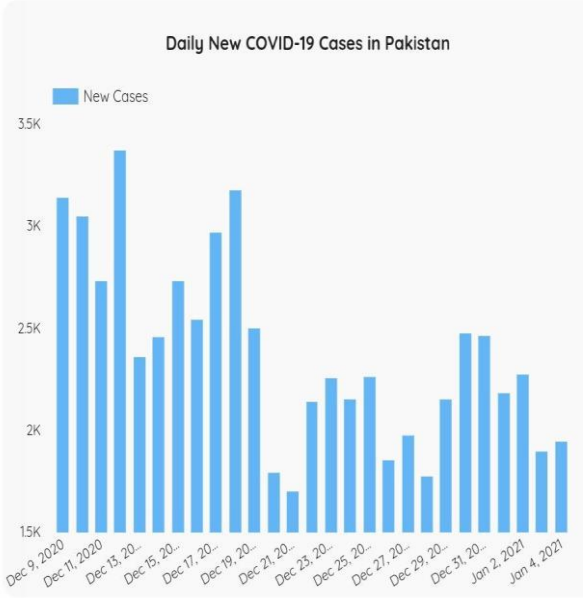

Figure-2: Daily Covid-19 Cases in Pakistan till the first week of January 2021 (https://covid.gov.pk/stats/pakistan)

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Original Article

IMPACT OF INGUINAL SENTINEL LYMPH NODE BIOPSY (SLNB) ON LONG TERM SURVIVAL OF PATIENTS WITH LOWER EXTREMITY MALIGNANT MELANOMA: A RETROSPECTIVE REVIEW

Sobia Manzoor[1], Ahmad Faraz Bhatti[2], Sami Ullah[3], Saima Tabassum[4], Ehsan Ahmed Khan[5]

ABSTRACT

Background: Sentinel lymph node biopsy (SLNB) is widely accepted as the standard of care for correct lymphatic basin staging for patients with clinically localized malignant melanoma. Herein, our experience of determining the impact of inguinal SLNB on node-negative, primary cutaneous melanoma of lower extremity in terms of long-term survival will be presented.

Methods: In this study, we retrospectively reviewed data of patients having lower extremity melanoma with Breslow thickness < 4 mm, who underwent inguinal SLNB (ISLNB) from January 2013 to January 2015 with follow up till January 2020, retrieved from hospital database software (EX-07-02-19-01). We collected demographic, primary disease data, surgery data, histological data, and outcome data during a 5-year follow-up.

Results: Of the 22 patients who underwent SLNB from 2013 to 2015, 13 (59.1%) patients had positive inguinal SLNB. The mean age of patients was 40 years, with more chances of positive SLNB (8 out of 13) in patients of age ≤ 45 (*p* value 0.019). Mean ±SD tumor Breslow thickness was 2.57 ± 0.86 (*p* value 0.0034). The mean follow-up period after surgery was 72.3 months (6.02 years). The mean ±SD number of days of hospital admission at the time of surgery was 3.7 ± 1.2 days (*p* value 0.037). The total number of OPD visits during the first year follow up were less in Inguinal SLNB negative patients (*p* value 0.097).

Conclusion: SLNB can be used as a routine procedure in node-negative malignant melanoma of the lower extremity for better survival and quality of life with fewer complications.

Key Words: Sentinel lymph node biopsy, Melanoma, Lower extremity

INTRODUCTION

Malignant melanoma is one of the most fatal cutaneous malignancies and is the most common malignant skin tumor of the foot. It is thought that lower extremity melanoma may be associated with poorer prognosis as its diagnosis is delayed due to its similarity with certain common ulcerative conditions, painlessness, and difficult position for every patient to visualize.[1] It can arise from any melanin-containing cell of the body and spreads primarily by the lymphatic system. Therefore, regional lymph node metastasis is the most important outcome parameter in melanoma patients. It determines the risk of recurrence and mortality after surgical excision of melanoma.

Currently, wide local excision (WLE) and sentinel lymph node biopsy (SLNB) is widely accepted as the standard of care for correct lymphatic basin staging for patients with clinically localized malignant melanoma.[2] Because the sentinel lymph node (SLN) is the first site of regional metastasis, its tumor status accurately predicts the tumor status of other nodes in the lymphatic basin.[3] The effectiveness of SLNB is directly related to both patient and tumor characteristics including age, sex, site of the tumor, depth of invasion, ulceration, and vascular invasion. It is done as routine management in patients with melanoma ≥1 mm depth of invasion and may be considered for thin lesions with high-risk characteristics (e.g. ulceration,

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lymphovascular invasion, high mitotic rate).[4] Having shown both the staging accuracy and pathological specificity of the SLNB technique, Morton et al. postulated that this minimally invasive alternative to radical regional lymphadenectomy could not only reliably identify patients with clinically occult nodal metastasis, but would also favorably affect the oncological outcomes.[5] However, the impact of SLNB on the long-term survival of patients with melanoma in terms of clinical and histopathological characteristics has yet to be established. Also, there is a scarcity of studies on lower extremity melanoma and its outcome after surgery specifically in our population. This study aims to determine the impact of inguinal SLNB on clinically localized, node-negative, primary cutaneous melanoma of the lower extremity in terms of long-term survival.

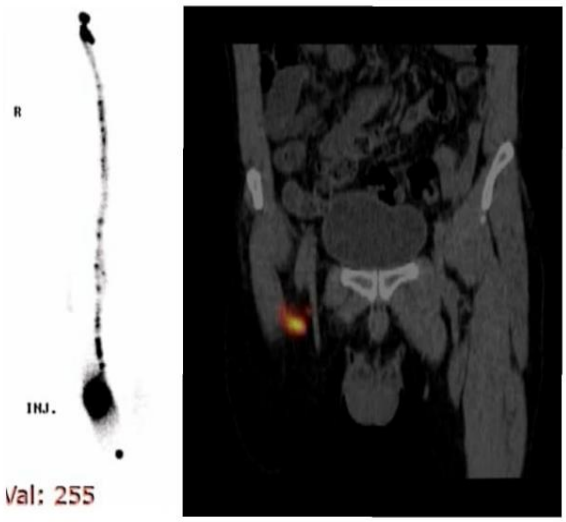
MATERIAL AND METHODS

This retrospective cohort study was conducted in the Surgical Oncology Department of Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC), Lahore, Pakistan. After approval from the Institutional Review Board (EX-07-02-19-01), data of patients who underwent inguinal sentinel lymph node biopsy for lower extremity melanoma from January 2013 to January 2015 with follow-up till January 2020 was retrieved from the hospital database software. Patients, age 15-75 years having biopsy-proven <4mm deep melanoma of lower extremity with no palpable inguinal lymphadenopathy on presentation, were included in the study. Patients, with age <15 years, having Breslow thickness >4mm, microscopic satellite lesions, distant metastasis, or recurrent disease were excluded from the study. Patients who had melanoma excision outside our hospital were also excluded.

It was found all the study patients were admitted to the hospital one day before surgery and had a subcutaneous injection of technetium-99m (^{99m}Tc) labeled filtered sulphur colloid in four quadrants near the tumor, on the morning of surgery. Dynamic imaging of drainage pattern from the primary lesion was made using scintillation camera in 1-30 min after injection followed by delayed whole-body imaging. During surgery, a handheld gamma probe (Neoprobe^{TM} GDS, Gamma detection system) was used to identify sentinel lymph nodes [Figure-1]. The sample lymph nodes were sent for frozen section and the decision of complete inguinal lymph node dissection was made in patients with sentinel lymph nodes positive for micrometastasis.

Figure-1: Gamma detection system with a handheld probe

We collected demographic, primary disease data (duration of the tumor, site of the tumor, tumor size, Breslow thickness, and presence of ulceration), surgical data (Tumor excision margin, thickness, and post-operative complications), histological data (tumor margin clearance achieved, histological subtype, number of SLN and number of positive lymph nodes), and outcome data (recurrence, metastasis, and mortality) during 5-year follow-up. To assess morbidity, the number of days of hospital stay and number of hospital visits during the first-year post-operative was also recorded.



(a) (b)

Figure-2: Inguinal sentinel lymph node identification using lymphoscintigraphy and SPECT/CT in a patient with melanoma right foot

(a) Lower extremity image showing tracer drainage from injection site with visualization of lymphatic ducts towards the inguinal lymph nodes.
(b) Further localization of sentinel lymph nodes on SPECT/CT scan with volume rendering.

Descriptive variables were presented by proportions, mean or median values, and percentage as appropriate by data distribution. Age (15-45 or 46-75 years) and Breslow thickness (≤2.0 or 2.1-4.0 mm) were dichotomized. In SLNB positive and negative patients, categorical variables like age, gender, Breslow thickness, ulceration, and outcome measures like recurrence were compared using the chi-square test. Data of variables like duration of melanoma, anatomical site of melanoma, histological subtype, complications, metastasis, number of days of hospital stay, and number of hospital visits during 1st year after surgery were compared in SLNB positive and negative patient by t-test. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) 21.0 statistical software. Statistical significance was defined as p value <0.05.

RESULTS

There were 22 patients who presented with biopsy-proven, node-negative lower extremity malignant melanoma and underwent excision and inguinal SLNB from January 2013 to January 2015. Among them, 13 (59.1%) patients had positive inguinal SLNB and 9 (40.9%) patients had a negative inguinal SLNB. The mean follow-up period after surgery was 72.3 months (6.02 years) with a range of 62.7-83.7 months (5.2-6.98 years).

The mean (SD) age of patients at the time of presentation was 40 ± 9.3 years, of which 12 (54.5%) were males. The median patient age was 40 years in ISLNB positive group and 44 years in ISLNB negative group. Patients with age ≤ 45 years were more likely to have a tumor with positive ISLNB (8 out of 13) and it was found to be statistically significant (p=0.019). Mean (SD) total duration of melanoma at the time of presentation was 12 ± 7 months.

The most common site of melanoma was foot 14 (63.6%), followed by leg 3(13.6%), thigh 2(9.1%), knee and popliteal fossa 2(9.1%), and ankle 1(4.5%). Mean (SD) size of tumor (Length x width) was 4 ± 1.5 x 3 ± 1.1 cm. Mean (SD) tumor Breslow thickness was 2.57 ± 0.86 and 17 (77.3%) tumors had ulceration. Most common melanoma subtype was superficial spreading in 10 (45.4%), nodular in 5 (22.7%), acral lentiginous in 4 (18.2%), lentigo maligna in 2 (9.1%) and desmoplastic melanoma in 1 (4.5%). In 5 (22.7%) of patients, melanoma arisen from pre-existing nevus while 1 (4.5) arisen from post-burn scarring. There was no statistically significant difference in ISLNB positive and negative patients in distribution according to gender, anatomical site, ulceration, and tumor subtype. (Table 1).

Table-1: Demographic, clinical, and histopathological data of patients with positive and negative Inguinal sentinel lymph node biopsy (ISLNB).

Demographic, clinical, and histopathological characteristics	Positive ISLNB patients (%)	Negative ISLNB patients (%)	p-value
Age 15-45 years (n=14) 46-75 years (n=8)	 8 (36.4) 5 (22.7)	 6 (27.3) 3 (13.6)	 0.33 0.019
Gender Male (n=12) Female (n=10)	 6 (27.3) 7 (31.8)	 6 (27.3) 3 (13.6)	 0.34 0.61
Anatomical location Thigh (n=2) Knee and popliteal fossa (n=2) Leg (n=3) Ankle (n=1) Foot (n=14)	 1 (4.5) 2 (9.1) 3 (13.6) -- 7 (31.8)	 1 (4.5) -- -- 1 (4.5) 7 (31.8)	0.45
Melanoma arising from the previous nevus	3 (13.6)	2 (9.1)	
Melanoma arising from post-burn scar	1 (4.5)	---	
Breslow thickness ≤ 2.0 mm (n=9) 2.1 – 4.0 mm (n=13)	 2 (9.1) 11 (50)	 7 (31.8) 2 (9.1)	 0.0034
Ulceration Yes (n=17) No (n=5)	 11 (50) 2 (9.1)	 6 (27.3) 3 (13.6)	 0.32
Melanoma subtype Superficial spreading (n=10) Nodular (n=5) Acral lentiginous (n=4) Lentigo maligna (n=2) Desmoplastic melanoma (n=1)	 8 (36.4) 2 (9.1) 2 (9.1) -- 1 (4.5)	 2 (9.1) 3 (13.6) 2 (9.1) 2 (9.1) --	 0.28

The range of resection margin was 10-20 mm according to proximity to vital structures. Mean margin clearance achieved after tumor resection was 9.2mm (Range 5-15mm). Number of SLN sent for frozen section was 2 in 12 (54.5%) and 1 in 10 (45.5%). Inguinal SLNB was positive for tumor cells in 13 (59.1%) and negative in 9 (40.9%) patients. Completion inguinal lymph node dissection (CILND) with Saphenous sparing and Sartorius muscle transposition was done in SLNB positive patients after confirmation by frozen section during the same surgery. To reduce the risk of lymphedema, all patients undergoing CILND, were advised to use compression garments for at least 6 months postoperatively.

ISLNB negative patients had a few complications as compared to ISLNB positive patients. No complication was seen in 14 (63.6%) patients with partial graft loss in 4 (18.2%), wound dehiscence in 2 (9.1%), seroma formation after complete inguinal lymph node dissection (CILND) in 2 (9.1%), and flap tip necrosis in 2(9.1%). Lymphedema did not develop in our study patients. (Table 2).

Table-2: Distribution according to complications in Inguinal SLNB positive and negative patients.

Complications (n=9)	ISLNB positive patients (%)	ISLNB negative patients (%)
Partial graft loss (n=4)	3 (13.6)	1 (4.5)
Infection and wound dehiscence (n=2)	2 (9.1)	--
Seroma formation (n=2)	2(9.1)	--
Skin flap tip necrosis (n=2)	2(9.1)	--
No complications (n=14)	6 (27.3)	8 (36.4)

It was observed that patients with negative SLNB had a better outcome. Local recurrence in the form of the nodule/non-healing ulcer near or under the previous tumor resection site was seen in 6 (27.3%) patients within mean (SD) time of 3.16 ± 1.5 months. Out of the 5 (22.7%) patients were SLNB positive while only 1 (4.5%) was SLNB negative. Recurrence in the regional lymph nodes (Inguinal) occurred in 2 (9.1%) patients who were SLNB negative. Distant metastasis occurred in 11 (50%) patients (not significant, *p* value 0.19). The mean (SD) number of days of hospital admission at the time of surgery was 3.7 ± 1.2 days (significant, *p* value 0.037). Out of 22 patients, 11 (50%) required additional hospital admission for 14 ± 5.4 days (range

6-25 days) for management of surgery or outcome (recurrence and metastasis) related complications (not significant, *p* value 0.46). The total number of OPD visits during the first-year follow-up was less in Inguinal SLNB negative patients i.e, 7.7 ± 3.7 compared to 10 ± 4.14 in Inguinal SLNB positive patients (significant, *p* value 0.097). It was also observed that 11 (50%) remained alive and disease-free even after a mean follow-up period of 72.3 months (6.02 years) after surgery, with additional 4 (18.2%) patients alive after chemotherapy for recurrence or metastasis. Mortality of 7 (31.8%) SLNB positive patients occurred after a mean time period of 8.4 ± 3.4 months during treatment. No death occurred in SLNB negative patients. (Table 3).

DISCUSSION

SLNB is a minimally invasive technique for the detection of metastatic melanoma in a targeted fashion using radioisotopes. It was first described by Morton and colleagues in 1992.[6] With the refinement of the technique, its reliability and acceptance have increased worldwide. In this observational study, the impact of SLNB on survival outcome of lower extremity melanoma patients was studied in relation to clinicopathological characteristics. It was noticed that in patients with age 45 years and younger, the risk of lymph node involvement became higher which was comparable with the results of other studies.[7] In our patients, it was most likely associated with a longer duration of melanoma and delay in seeking treatment. After the diagnosis of melanoma by incisional biopsy, the single most important factor that determines further management course is the thickness of the melanoma.[8] Various studies have shown that Clarks levels are only prognostic for <1mm thick melanoma.[9] In most of our cases melanoma thickness was >1mm at the time of presentation due to delayed presentation and diagnosis. Therefore, in this study, Breslow thickness was considered.

There are no defined criteria to identify these lower extremity melanoma patients who have more chances to have positive SLNB results. Most guidelines suggest considering SLNB for melanomas with pathologic stage T1b and above, as well as T1a melanomas with high-risk features.[10] In the present study, all

Table-3: Outcome in both inguinal SLNB positive and negative patients.

Outcome measures (n= number of patients)		**ISLNB positive patients (%)**	**ISLNB negative patients (%)**	***p*- value**
Recurrence (n=8)	Local nodule (satellite or in transit) (n=6)	5 (22.7)	1 (4.5)	---
	Regional nodal basin (n=2)	--	2(9.1)	
Metastasis (n=11)	Pelvic Lymph nodes (n=8)	7 (31.8)	1 (4.5	0.19
	Pulmonary (n=9)	7 (31.8)	2 (9.1)	
	Hepatic (n=1)	1 (4.5)	--	
	Peritoneal (n=1)	1 (4.5)	--	
Morbidity and mortality	Mean ± SD number of days of hospital admission after surgery (n=22)	4 ± 1.3 (n=13)	3 ± 0.5 (n=9)	0.037
	Mean ± SD number of additional days of hospital admission during the first year after surgery (n=11)	14 ± 6 (n=8)	13.7 ± 3.3 (n=3)	0.46
	Mean ± SD number of OPD visits during the first year follow up	10 ± 4.14 (n=13)	8 ± 3.7 (n=9)	0.097
	Number of patients alive without disease (n=11)	5 (22.7)	6 (27.3)	0.47
	Number of patients who are alive after receiving chemotherapy (n=4)	1 (4.5)	3 (13.6)	
	Number of patients who died during treatment (n=7)	7 (31.8)	--	

melanoma patients with <4mm thickness and clinically no palpable inguinal lymph nodes were included. It was found that positive SLNB results were directly related to increasing Breslow thickness and ulceration. It was also observed that delayed presentation in seeking medical advice for developing lesion resulted in deeper melanoma with Breslow thickness ranging from 2.1-4.0 mm in 13 (59.1%) patients.

Sladden et. al. reported equivocal results for wider versus narrower margins of melanoma excision in their systematic review.[11] The same finding was implemented by taking a narrow margin (10 mm) near the heel pad and the wider margin (20 mm) elsewhere. Regarding anatomical location, it was seen that the foot was the most common site of presentation in the lower extremity. Some studies showed that up to one-third of total body melanoma presentation occurs in the foot or distal lower extremity.[12]It was also observed that superficial spreading melanoma was the most common primary histological subtype 10 (45.5%) which was consistent with findings of several other studies.[13]

It is proven now that surgical morbidity of SLNB is very low as it is minimally invasive compared to complete inguinal lymph node dissection (CILND). All the patients with positive SLNB results (13 (59%) in our study) underwent CILND to achieve regional control. It does not reduce the risk of further spread of tumor but reduces disease burden. To reduce the risk of lymphedema, saphenous vein sparing inguinal lymph node dissection with sartorius muscle transposition was done in all patients.[14,15] In the postoperative period, all patients who underwent complete inguinal lymph node dissection were advised compression garments and lymphatic drainage massage for at least 6 months to reduce the risk of lymphedema[16]. Various studies show complications rate of up to 71-77% after CILND with seroma formation in 46%.[17] Overall complication rate in our patients was 41%, including partial graft loss, infection and wound dehiscence, seroma formation, and skin flap tip necrosis. Most of these complications were seen in SLNB positive patients (36.4%) and were associated with CILND. One of the SLNB negative patients 4.5% patient had partial graft loss which healed by conservative management.

In literature, it is described that the chance of recurrence in SLNB negative patients ranges from 9-24%[18,19] which was found to be 4.5% in our study. It is thought to be associated with primary hematogenous dissemination instead of lymphatic spread.[20] Certain prognostic factors such as increasing age, thicker primary tumor, ulceration, nodular subtype[21,] and the location at foot[22] were found to be associated with a high risk of recurrence. Recurrence at the primary tumor site was mostly seen in SLNB positive patients (22.7%) and was associated with deep, ulcerated melanoma (Mean Breslow thickness 3mm).

In our study, 9.1% of SLNB negative patients later on developed regional lymph nodal metastasis which was consistent with the range of 3-11% given by various studies.[23] It was also seen that 13.6% of our SLNB negative patients developed pelvic lymph node and distant metastasis after ILND which was diagnosed at 6 months follow up with CT chest, abdomen, and pelvis. Also, distant metastasis developed in 36.4% of SLNB positive patients who underwent CILND at the time of tumor extirpation. It can be explained by the concept of primary hematogenous spread as described earlier.[24]

With respect to morbidity, the low rate of surgery-related complications and metastasis in 31.8% of SLNB negative patients resulted in a reduced need for the hospital stay and OPD visits. Those SLNB negative and positive patients (18.2%) who had chemotherapy for distant metastasis and were alive even after five years of follow-up, had to visit the hospital more frequently for the treatment of surgery and chemotherapy-related complications leading to prolonged morbidity. It was also observed that the disease-free survival rate markedly reduced with the presence of positive sentinel lymph node and increased thickness of the primary

tumor. A high mortality rate was seen in SLNB positive patients (31.8 %). In our study, 5-year survival was 68.2% which was comparable with the range 51-87% of various studies.[25]

Our study has certain strengths and limitations. The main strength of our study is that it gives a detailed analysis of demographical, clinical, histopathological, and follow-up data with respect to SLNB negative and positive results. It also gives thorough information about the surgical approach for the excision of melanoma and regional lymph node management in our patients. Also, high-quality follow-up data in terms of recurrence, overall morbidity, and mortality is measured in detail.

Limitation of study

The main limitation of our study is that it is a retrospective cohort from a single-center leading to more chances of selection bias. The patient number was also small and results were based on a relatively short follow-up period (5 years instead of 10 years). There are different imaging and lymphoscintigraphy protocols to identify sentinel lymph nodes therefore, our study results cannot be generalized.

CONCLUSION

SLNB is a minimally invasive technique that can help early detection of lymphatic spread of lower extremity melanoma. By making it a routine procedure in node-negative malignant melanoma of the lower extremity, a better outcome can be achieved in terms of survival and quality of life with fewer complications, a smaller number of hospital admission days, and OPD visits.

AUTHOR'S CONTRIBUTION

SM: Main researcher
AFB: Supervisor of the research work
SU: Helped in data collection and writing
ST: Data analysis and performed analytical calculations
EAK: Data collection and performed computation

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Original Article

GENDER BASED DIFFERENCES IN KNOWLEDGE AND PERCEPTIONS OF CONTRACEPTIVE METHODS AMONG UNDERGRADUATE MEDICAL STUDENTS IN LAHORE.

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ABSTRACT

Background: Pakistan is the sixth most populous country in the world with low contraceptive prevalence rate (34%) and high unmet need for family planning (17.2%). This study was carried out to assess the knowledge of contraceptive methods among medical students and to highlight the importance of family planning methods through effective family education program in both young males and females of Pakistan.

Material & Methods: A cross-sectional survey was conducted among students of Akhtar Saeed Medical and Dental institutions and a sample of 240 participants was collected through non-probability convenience sampling technique. After IRB clearance, a structured questionnaire was given to the participants for data collection. First year students from MBBS, BDS, DPT, Pharm D and nursing, who gave the informed consent and were willing to participate, were included in the study. Data was analyzed using SPSS version 23. Bivariate analysis was conducted to assess the gender difference in knowledge regarding contraceptive methods in students by keeping p value less than 0.05 as significant.

Results: This study included 240 students, out of which, 83(34.6%) were males and 157(65.4%) were females. It was observed that females had better knowledge and understanding of natural, temporary and permanent methods of contraception with significant p value = 0.00. Females were more in favour of use of contraceptive methods in future with p value = 0.00 and they had more knowledge of uses of oral contraceptive pills with p value < 0.00. It was found out during the survey, that raised family income/month was directly proportional to the better knowledge level regarding all types of contraception with p value < 0.05. Parent's educational status had also positively affected the knowledge of contraceptive methods of participants of this study.

Conclusion: A significant difference was observed in positive knowledge of female students regarding contraceptive methods. However, no significant difference among male and female students was found regarding barriers in contraceptive use and their satisfaction levels toward need of improvement of family planning services in Pakistan.

Key Words: Contraceptive methods, Knowledge, Family planning

INTRODUCTION

Contraceptive methods are preventive methods to avoid unwanted pregnancies. It includes intrauterine contraceptive devices (IUCD), barrier methods (condoms), hormonal methods, emergency contraception pills and implants etc.[1]

Each year, about 68000 women die because of unsafe abortions and millions of women end up with many complications of unsafe abortions, which include severe infections and bleeding.[2] Family planning is the most important health intervention of twentieth century.[3]

It has been estimated that the global population will increase to 9.5 billion in 2050.[4] However, in 2013, Pakistan has become the sixth largest country with population of 191 million.[5] Urban population with low income does know the importance of small family size, but 'less contraceptive usage' due to less education, discontinuation of method and improper knowledge.[6]

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Contraceptive use among young women (aged 15-24) is lower than among relatively older women in the developing world.[7] Globally, youths are more sexually active than any subgroup of the population.[8] It is considered as a period of vulnerabilities, in terms of both biological (physical and psychological) and environmental aspect.[9] Their sexual behavior has been recognized as an important social and health concern in the developing world.[10] Around 70,000 women aged 15-19 years die each year of pregnancy and child birth causes. More than 18 million young women give birth to a baby each year and among them 9 out of 10 are living in developing countries.[11] About 30% women give birth to the first child before their 20th birthday. Making young women aware of emergency contraceptives help to prevent unwanted pregnancies and promote safe sex. Sexually active young women are clients with special needs for contraception.[12]

With the influx of western culture, our society is becoming more liberal with regards to sexuality. Traditional religious and moral concepts, self-esteem and educational level, no longer play a leading role in restricting this behaviour.[13] In India, average age of first sexual encounter is 17-18years. However, majority of students lack awareness of the harms of unsafe sex. Most of them resort to quacks or untrained doctors for abortion when they get pregnant, leading to unnecessary morbidity and mortality.[14]

The current study pursues a novel subject in Pakistani settings with objective of assessing the knowledge and ascertain if there is a need for pre-marital contraceptive counselling among male and female students of medical and Allied health professions. The escalating youth population predisposes these health issues and increases threats to their present situation. This study will guide the health planners to develop a more responsive and effective family planning education program through well-established information services and the need to incorporate gender issues in their interventional program for young males and females of Pakistan.

MATERIAL AND METHODS

A cross-sectional study was conducted, using structured questionnaire among undergraduate students of Akhtar Saeed Medical and Dental Institutions. This study was conducted from 1st March to 31stAugust, 2019. A sample of 240 participants was collected through nonprobability convenience sampling technique. All participants of more than 18 years of age of both genders, were included in the study. Before collection of data through a structured questionnaire, IRB clearance (Approval No: M-18/023/-CM) was obtained from Akhtar Saeed Medical and Dental college. Data was kept in custody of principal investigator and was kept confidential. Data was entered, coded and analyzed using SPSS version 23. Qualitative variables were presented in the form of tables, bar charts and pie charts.

Chi-square test was applied to find out association of variables with gender difference, keeping 95% confidence interval. P-value was fixed at$\leq$0.05 to declare results significant.

RESULTS

A total of 240 participants were included in the study and a vast majority of participants 157(65.4%) were females. The age group ranged from 18-22 years with mean age 19.2±0.9 years. 114(47.5%) participants were from Lahore and rest of them belonged to other cities. 47(19.6%) students were from MBBS, 51(21.3%) from BDS, 79(32.9%) from Pharm-D and 62(25.8%) were from Allied sciences. Eighty-two (34.2%) participants had family income more than 100,000 rupees/month. It was observed that knowledge of students regarding importance of sexual health education and different types of contraceptive methods were better with raised family income/month and educational status of both parents. Significant results were found with $p<0.05$.

Table-1: Socio-Demographic Profile.

Gender of respondents	**Frequency**	**Percentage**
Males	83	34.6
Females	157	65.4
Total	240	100
Respondents age in years	**Frequency**	**Percentage**
18	55	22.9
19	102	42.5
20	62	25.8
21	16	6.7
22	5	2.1
Total	240	100
Academic program of students	**Frequency**	**Percentage**
MBBS	47	19.6
BDS	51	21.3
DPT	1	0.4
PHARM-D	79	32.9
Allied Sciences	62	25.8
Total	240	100
Father's education	**Frequency**	**Percentage**
Illiterate	12	5
Primary	6	2.5
Matric	31	12.9
Intermediate	27	11.3
Graduate	87	36.3
Masters	77	32.1
Total	240	100
Father's job status	**Frequency**	**Percentage**
Employed	187	77.9
Unemployed	53	22.1
Total	240	100
Mother's education	**Frequency**	**Percentage**
Illiterate	16	6.7
Primary	19	7.9
Matric	37	15.4
Intermediate	46	19.2
Graduate	78	32.5
Masters	44	18.3
Total	240	100
Mother's job status	**Frequency**	**Percentage**
Employed	52	21.7
Unemployed	188	78.3
Total	240	100
Family income/ Month	**Frequency**	**Percentage**
<25000	24	10
<50,000	49	20.4
<1,00,000	85	35.4
>1,00,000	82	34.2
Total	**240**	**100**

Bivariate analysis was performed to assess the gender difference in knowledge and perception of the participants regarding different types of contraceptive methods. Statistically significant difference in knowledge and perceptions between males and females was found. Sixty (25%) students had knowledge about natural methods of contraception, out of which, 31(51.6%) were females. 122(50.2%) participants had

knowledge about temporary methods of contraception while 93(38.8%) had knowledge about permanent methods of contraception and 48(51.6%) among them were females. Significant difference in knowledge of male and female students was observed with p=0.00 was found. Sixty-four (27.1%) students knew about combined oral contraceptive pills. Among them, 31(48.4%) were females (p=0.00).

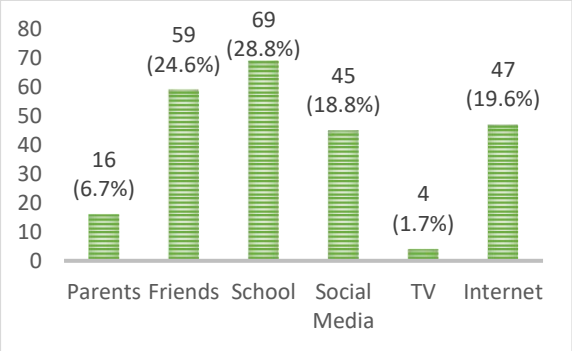

Figure-1: Sources of information of contraceptives

Regarding source of information of contraceptives, out of 240 participants, 16(6.7%) were informed by their parents, 59 (24.6%) by their friends, 69(28.8%) in schools and colleges, 45(18.8%) by social media, 4(1.7%) by TV and 47(19.6%) by the use of internet facilities.

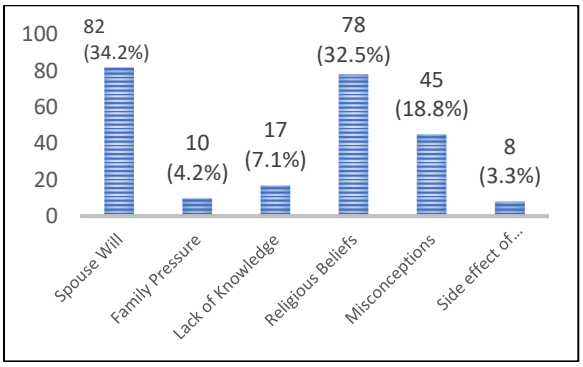

Figure-2: Important barriers of contraceptive use

Table-2:

Bivariate analysis of knowledge and perception of male and female students regarding contraceptive methods					
Variable	Males		Females		p-value
	Frequency	Percentage	Frequency	Percentage	
Knowledge regarding natural methods of contraception					
Yes	29	48.3	31	51.6	0.01*
No	54	30	126	70	
Knowledge regarding temporary methods of contraception					
Yes	63	51.6	59	48.3	0.00*
No	20	16.9	98	83.1	
Knowledge regarding permanent methods of contraception					
Yes	45	48.3	48	51.6	0.00*
No	38	25.8	109	74.1	
Knowledge regarding combined oral contraceptive pills					
Yes	33	51.5	31	48.4	0.00*
No	50	28.4	126	71.6	
Perception regarding use of contraceptives in future					
Yes	51	54.8	42	45.	0.00*
No	32	21.7	115	78.2	
Perception regarding need of improvement of family planning services in Pakistan					
Yes	61	32.2	128	67.7	0.14
No	22	43.1	29	56.9	
Perception regarding barriers to the use of contraceptive methods in our society					
Yes	61	38.6	97	61.4	0.06
No	22	26.8	60	73.2	
Perception in favour of use of contraceptive methods					
Yes	52	40.6	76	59.3	0.03*
No	31	27.6	81	72.3	

Perception of students regarding barriers to the use of contraceptives in our society revealed that, out of 240, 82(34.2%) thought spouse will is a barrier, 10(4.2%) thought family pressure, 78(32.5%) thought religious beliefs, 17(7.1%) thought lack of knowledge, 45(18.8%) thought misconceptions and 8(3.3%) thought side effects of contraception as a barrier.

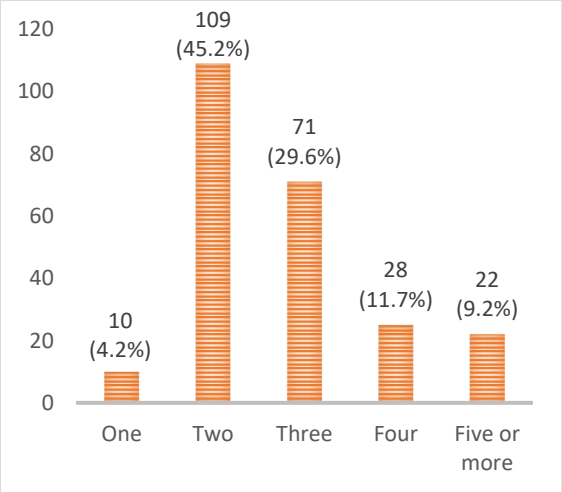

Figure-3: Perception regarding expected number of children in future

Out of 240 students, 10(4.2%) said that a couple should have one child, 109(45.2%) agreed to had two children, 71(29.6%) agreed to had three children, 28(11.7%) agreed to had four children and 22(9.2%) agreed to had five or more children in future.

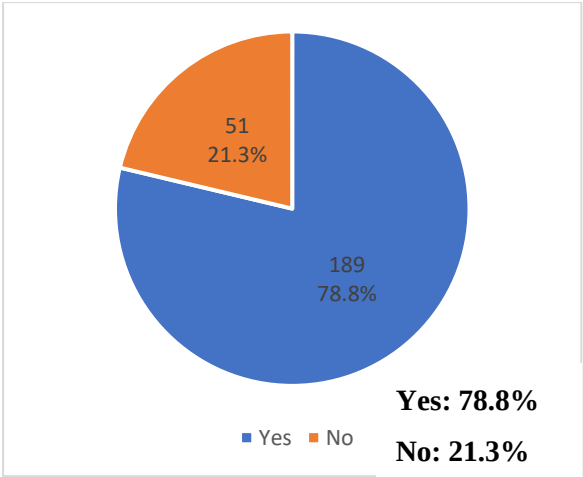

Figure-4: Availability of contraceptive services in Pakistan

Out of 240, 94(39.2 %) participants were willing to use contraceptive methods in future and 189(78.8%) students were in favour of need of improvement in family planning services in Pakistan. Among them, 128(67.7%) were females but no significant difference in opinion in both genders regarding improvement of family planning services in Pakistan was found(p=0.14).

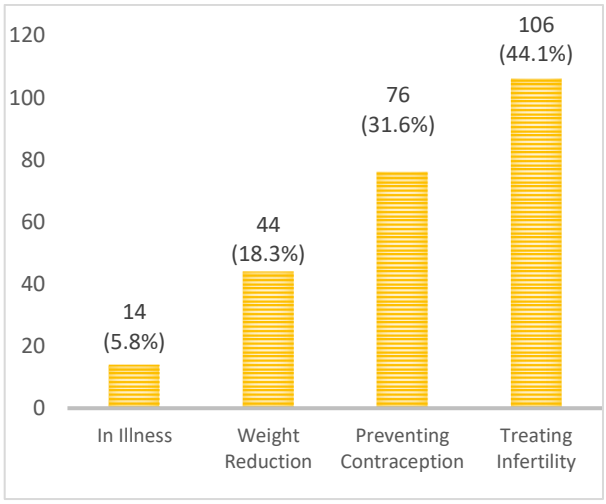

Figure-5: Knowledge regarding purpose of contraceptives usage

Out of 240 students, only 72(30%) knew about the significance of sexual health education. No significant difference was observed among males and females about their opinion on importance of sexual health education (p=0.11). Knowledge regarding purpose of use of oral contraceptive pills showed that out of 240 students, 14(5.8%) thought that they were used in illness, 44(18.3%) thought that they were used for weight reduction, 76(31.6%) thought that they were used for preventing conception, 106(44.1%) thought that they were used for treating infertility. Significant difference in knowledge of both genders was found with p=0.05.

DISCUSSION

Every year unplanned pregnancies lead to atleast 50 million abortions world-wide and result in approximately 80000 maternal deaths.[15] Around 25 million unsafe abortions take place every year in almost all developing

countries.[16] Family planning promotion is priority for the government of Pakistan to keep pace between socio-economic growth and population expansion.[17]

This survey included 240 respondents, out of which, 34.6% were male and 65.4% were females. In another study in Ghana, 53% were male and 47% were female.[18] In this study, out of 240 respondent's, 72(30%) had received sexual health education. In another study in college students of Kathmandu Nepal, 27.8% students had received reproductive health education while 76.3% had not received any education.[19] In this survey, 14(5.8%) students considered the use of contraceptive for illness, 44(18.3%) for weight reduction, 76(31.6%) thought of contraceptives to be used for preventing conception and 106(44.1%) considered it for treating infertility. In contrast to this, in another study in Ghana, 66.67% students had knowledge that contraceptive methods were used to prevent pregnancy and to prevent sexually transmitted diseases, 22.22% had knowledge that contraceptives are used to prevent child birth, 5.56% thought that these were used to prevent abortion, 5.56% thought that they were used for family planning.[20] According to another study in female undergraduates in Tanzania, 92.2% had knowledge that contraceptive methods were used to prevent pregnancy and 85.6% students had knowledge that contraceptive methods were used to prevent STDs, 90.7% thought that these were used for family planning.[21] It revealed the fact that females had better understanding of uses of contraceptives. Similar findings were observed in this study as well.

This survey showed that out of 240 respondents, 122(50.8%) students had knowledge about contraceptives. 78(32.5%) knew about condoms, 36(15%) knew about hormonal pills, 4(1.7 %) knew about injectables, 1(0.4%) knew about implants, 2(0.8%) knew about IUCD and 1(0.4%) knew about ligation. In another cross-sectional study in Uganda, 86.7% students had knowledge about hormonal pills, 35% had knowledge about IUCD, 50.3% had knowledge about injection, 26.7% had knowledge about implants, 88.4% had knowledge about male condoms, 22.1% had knowledge about female condoms,7.3% had knowledge about diaphragm and 3.5 % had knowledge about foam.[22] In another study in students of Ghana, 55.56% students had knowledge about condoms, 27.78% had knowledge about pills, 5.56 % had knowledge about IUCD, 5.56% had knowledge about spermicidal cream and 5.56% had knowledge about withdrawal.[23] In a study in Tanzania, 88% students knew about condoms, 83.5% knew about pills, 59.8% knew about injectable pills, 37.2% knew about implants, 29.7% knew about loops and 26.1% knew about tubal ligation.[24]

This study revealed the fact that only 93(38.8%) students had knowledge about permanent method of contraception, out of which, 45(48.3%) were males and 48(51.7%) were females. 65(27.1%) students had knowledge about combined oral contraceptives, out of which, 33(51.5%) were males and 31(48.4%) were females. Contrary to this survey, another study in Ethiopia showed that only 29.5% of students had knowledge about combined oral contraceptives.[25] In another study in Nicosia, only 28.9% students had knowledge about combined oral contraceptives.[23]

During this survey, it was found that 64(26.7%) students had knowledge about progesterone only pills and 60(25%) students had knowledge about natural methods of contraception, out of which, 29(48.3%) were males and 31(51.6%) were females. 205(85.4%) students knew about rhythm method, 12(5%) knew about coitus interruptus, 11(4.6%) knew about breast feeding as a method of natural contraception and only 12(5%) students had knowledge about basal body temperature. However, a study in Uganda showed that 3.6% students had knowledge about lactational amenorrhea, 10.2% had knowledge about rhythm method, 34.2% had knowledge about withdrawal.[22] In contrary to this, a study showed that 25.4% students had knowledge about withdraw 31.8% had knowledge about breast feeding,

and 36.5% had knowledge about periodic abstinence.[23]

This study showed that 16(6.7%) students got information regarding contraceptives from their parents, 59(24.6%) from their friends, 69(28.8%) from school, 45(18.8%) from social media, 4(1.7%) from TV and 47(19.6%) students received it from Internet. Whereas, a study in

Uganda showed that 3.3% students got information from their parents, 30% from their friends, 6.7% from their brothers or sisters and 60% from TV/radios.[26] During this survey, 94(39.2%) students said that they would consider the use of contraceptives in future, out of which 51(54.8%) were males and 43(45.2%) were females. In comparison to this, another study showed that 12.3% students would consider using contraceptive methods in future.[24]

CONCLUSION

Reproductive health knowledge among male adolescents was comparatively less than that of their female peers. Female students appeared to be significantly more knowledgeable than the male adolescents about contraceptive methods. This survey showed that strategies to promote use of contraception should be focused on spreading accurate information through medical and informational sources to prevent unnecessary morbidity and mortality due to unsafe abortions.

RECOMMENDATIONS

Current reproductive health and HIV prevention programs should take into account gender-based double standards among young people and their unmet reproductive health needs. Increasing modern contraceptive usage requires community-wide, multi-faceted interventions and the combined provision of information, skills, support and access to youth friendly services by the Government. Intensive education on contraceptive use should be provided at a much earlier level of education, ie. during primary school and secondary school, before the adolescents are sexually active.

AUTHOR'S CONTRIBUTION

IQ: Conceptualization & data interpretation
IM: Analysis of results & overall supervision
HM: Write up of discussion
AMJ: Literature review & methodology review
FHR: Data collection

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Original Article

SERUM TESTOSTERONE AND FOLLICLE STIMULATING HORMONE/LEUTINIZING HORMONE RATIO IN WOMEN HAVING HIRSUTISM

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ABSTRACT

Background: Idiopathic hirsutism is on the rise in the local female population. The objective of this study was to determine the role of testosterone, follicle-stimulating hormone/leutinizing hormone ratio in mild and moderate hirsutism.

Material and Methods: Sixty hirsute subjects aging 18-35 years were selected while ten normal healthy females were included as controls. An assessment of excess terminal growth of all subjects was made using the modified Ferriman and Gallwey scoring method. The hirsute subjects were categorized into mild and moderate hirsutism. Serum Testosterone, Follicle stimulating hormone, and luteinizing hormone levels were assayed by the ELISA technique.

Results: Serum testosterone was lower, non-significant, in hirsute subjects in comparison with control subjects. The follicle stimulating hormone/leutinizing hormone ratio was non significantly higher in hirsute subjects as compared to control subjects.

Conclusion: The findings suggest that hirsute women are suffering from idiopathic hirsutism.

Key Words: Hirsutism, Testosterone, ELISA technique

INTRODUCTION

Based on the structure, hair is divided into three types: lanugo, vellus, and terminal. Terminal hair includes eyebrows, eyelashes, scalp hair, axillary hair, pubic hair, and body and facial hair in men. Hirsutism is defined as excess terminal hair that appears in a male pattern in women. Based on visual examination of hair type and growth, various scoring methods have been elaborated, differing mainly according to the area of the body being examined.[1] The modified Ferriman Gallwey (mFG) scoring method, proposed by Hatchet al., scores 9 of the 11 body areas (upper lip, chin, chest, upper and lower back, upper and lower abdomen, arm, forearm, thigh, and lower leg) except lower legs and forearms as these are the areas sensitive to low androgen levels even in normal women. The total score ranges from 0-36.

If the presence of hirsutism is established or another evidence point to a history of hirsutism, diagnostic efforts should be focused to identify the underlying cause. It is important to perform a detailed evaluation in women having mild hirsutism because the severity of hirsutism does not always correlate with increased androgen levels.[2,3] Some patients with polycystic ovary syndrome (PCOS) or congenital adrenal hyperplasia may be having greatly increased androgen levels but no hirsutism at all. On the other hand, women with severe hirsutism may be having normal androgen concentrations. Even increased mild hirsutism in women may indicate an underlying increased androgen disorder.[4,5] Idiopathic hirsutism encompasses a distinct group of hirsute patients having normal androgen levels, ovaries, and ovulatory cycles. The mechanisms underlying hirsutism in these women may include increased conversion of testosterone into dihydrotestosterone and/or enhanced activity of androgen receptors. It is quite evident that research is mostly focused on PCOS while exploring androgen excess disorders, as the

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idiopathic hirsutism remains a less known possibility. In this regard, a realization of the fact that a large population of women is having idiopathic hirsutism will help to provide recommendations for screening and management of these patients.[6] This study was carried out to study the role of testosterone, Follicle stimulating hormone/ Leutinizing hormone (FSH/LH) ratio in the expression of idiopathic hirsutism in the local female population.

MATERIAL AND METHODS

This was a case-control study performed at the Institute of Molecular Biology & Biotechnology, University of Lahore, on 60 hirsute female subjects and 10 normal healthy females aged 18-35 years.

Inclusion criteria included subjects with an mFG score of eight or more, amenorrhea, ovulatory disorders, increased hair growth, virilization, alopecia, and acne. Exclusion criteria included subjects with an mFG score less than 8, pregnant or lactating women, subjects receiving oral contraceptives, drugs causing hirsutism, and drugs suppressing androgens in the last three months.

The study was approved by the Ethical Review Committee of the Institute of Molecular Biology & Biotechnology, University of Lahore. All the subjects completed a standardized history and clinical proforma, including questions about age, family history of hirsutism, onset and duration of the disorder, marital status, menstrual cycle length and regularity, other illnesses, and medications.

All subjects were assessed for increased terminal hair growth employing the modified Ferriman-Gallwey method. They were categorized into two groups: those with mild hirsutism (score 8-15) and those with moderate hirsutism (score 16-25).

The blood samples for total testosterone, follicle stimulating hormone, and luteinizing hormone assays were obtained by standard venepuncture technique; Three to four ml of venous blood was drawn from the cubital vein. The blood samples were centrifuged at 4,000 rpm and the serum samples were aliquoted and stored at -20^{o}C until used. The hormone assay was done by the ELISA technique.

The demographic variables were mentioned as simple descriptive statistics including standard error of means and standard deviation of numerical data like age, duration, modified Ferriman Gallwey (mFG) scores, and the serum hormone levels.

The significance of the difference between the groups was analyzed by independent samples t-test. p-value < 0.05 was considered statistically significant. All calculations were carried out with the SPSS version 17 (SPSS, Inc, Chicago, IL, USA).

RESULTS

Sixty hirsute female subjects were included in this study having ages from 18-35 years with a mean age of 24.58± 0.57 years. The age distribution of the studied subjects is shown in Table 1. All were hirsute in various degrees of the disorder. A batch of ten female subjects of matching ages with a mean value of 25.6 ± 1.76 years was also included in the study as the control group. The control group subjects had minimal hair growth on the face and limbs. There was neither any family history of hirsutism nor menstrual complaints in the control subjects.

In the control group, 80% of subjects were between 16-30 years of age. In the hirsute group, about 25% were of 16-20 years of age, however, more than 67% were between 21 to 30 years of age. Thus, overwhelmingly the sampled population was young and comparable between the control and hirsute groups.

Table-1. Age distribution of subjects in the control and hirsute groups.

Group	Age (Years) Group	Number	Average±SEM	%
Control	16-30	8	23.62±1.46	80
	31-35	2	33.5±1.5	20
Hirsute	16-20	15	19.4±0.21	25
	21-25	22	22.64±0.25	37
	26-30	18	28.28±0.39	30
	31-35	05	33.40±0.60	8

Table-2. Specific features of the hirsute subjects and the disorder.

	Duration in Years		Marital status		Menstrual Cycle pattern		Family History	
	1-5	6-11	Unmarried	Married	Regular	Irregular	Yes	No
No of Subjects	43	17	31	29	47	13	12	48
% in population	72	28	52	48	78	22	20	80

The general features include the duration of the disorder, marital status, family history, and history of the menstrual cycle.

About 25% of the subjects had hirsute symptoms up to a maximum of 5 years and less. The rest had the disorder for more than 5 up to 11 years. Thus, the study is largely focused on hirsutism of the younger population. The disease progressed slowly in all patients, developing over years. The range of the disease was from 1-14 years (Table 2) with a mean duration of 5.05 $\pm$ 2.59.

Twelve (20%) patients had family history of hirsutism. There were thirty-one (51.66%) unmarried patients and 29 (48.33%) married patients in the studied population. Out of sixty, forty-seven patients (78.33%) had regular menstrual cycles while thirteen patients (21.66%) had irregular menstruation.

Serum total testosterone level was 1.45±0.34; 1.05±0.12 and 0.96±0.10 nmol/L in the control, mild hirsute and moderate hirsute subjects respectively. The level of the hormone was 27.5% (p=0.230) lower in mild hirsute and 33.6% (p=0.202) lower in moderate hirsute subjects compared to the control subjects. However, the differences among the groups were not statistically significant. (Table 3 and Figure 1).

Table-3. Serum total testosterone levels in control group and hirsute group with mild and moderate hirsutism

Group		N	Mean (nmol/L)	% Change to Controls
Control		10	1.45±0.34	
Hirsute	**Mild**	51	1.05±0.12	-27.5
	Moderate	9	0.96±0.10	-33.6

(p > 0.05, Statistically not significant)

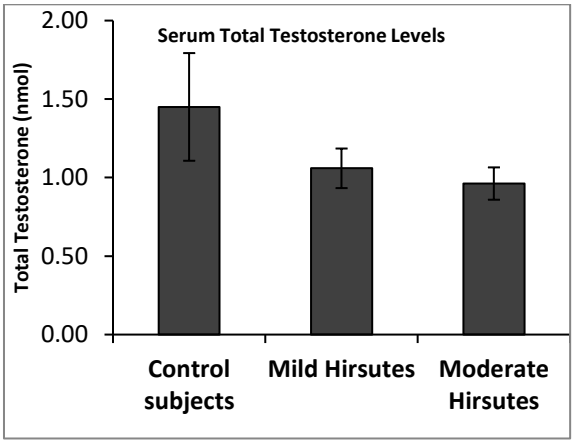
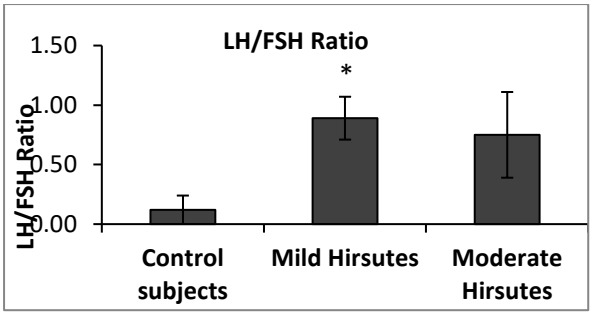


Figure – 1. Serum total testosterone levels in control subjects and hirsute subjects with mild and moderate hirsutism. (p > 0.05, Statistically not significant).

LH/FSH ratio was 0.12±0.12; 0.89±0.18 and 0.75±0.36 in the control, mild hirsute and moderate hirsute subjects respectively. The ratio was 86% (P=0.065) higher in mild hirsute and 84% (P=0.103) higher in moderate hirsute subjects compared to the control subjects. The differences among the groups were statistically non-significant. (Table 4 and Figure 2).

Table–4. LH/FSH Ratio in control group and hirsute group with mild and moderate hirsutism.

Group		N	Mean	% Change to Controls
Control		10	0.12±0.12	
Hirsute	**Mild**	51	0.89±0.18	86
	Moderate	9	0.75±0.36	84



Figure–2. LH/FSH Ratio in control subjects and hirsute subjects with mild and moderate hirsutism.

DISCUSSION

A rational diagnosis of hirsutism is important as it can point to several hormonal and other systemic disorders. Normally, 25% of young women have terminal hair on the face, areolae, or abdomen. This hair growth is governed by androgens and inherent hair follicle response to react to hormonal changes. The hair follicle response differs vastly in individuals causing the degree of hirsutism to match poorly with androgen concentrations.[3]

In females, testosterone originates from ovaries and adrenal glands. In pre-menopausal women, 50% of plasma testosterone is obtained equally from ovarian and adrenal secretion. The rest is synthesized from androstenedione in peripheral tissues including the adipose tissue.[7]

In this study, the mean age of subjects was 27.64±7.266; indicating that majority of the subjects were young. These results can be compared with other studies.[8,9] There was a slow progression of hirsutism in all subjects (mean duration was 7.52±6.217). There was no history of quickly developing the disease or severe virilization.

Concerning the severity of hirsutism; mild hirsutism (score 8-15) was present in 51 subjects (85%) and 9 subjects (15%) had moderate to severe hirsutism (score >15). In the current study, the chin, upper lip, and lower abdomen had higher mean mFG scores. On the other hand, the back and upper abdomen were involved less frequently. The mean hirsutism score in this study was 11.15±2.985. A mean hirsutism score of 13.5±4.6 was reported in a study on Kashmiri women.[10] A similar racial background may explain this similarity.

Serum total testosterone levels were found to be lower in hirsute subjects. Serum total testosterone levels showed no significant statistical difference between different categories. This finding is comparable with other studies showing fewer hirsute patients having increased androgen levels.[9] The hirsutism in our study population was therefore probably more of a peripheral origin at the follicular level. It is known that polymorphism of the androgen receptor gene also affects the receptor response to androgen androgens but reports regarding this effect have been inconsistent. Also, the response of the hair follicle to androgens differs greatly in individuals. Hirsutism is an interplay between circulating androgens, follicular androgen concentration, and the sensitivity of the hair follicle to androgens.[11]

The finding of statistically significant differences in LH/FSH ratios in predominantly young subjects with irregular menstrual cycles in our study draws attention to the possibility of a common and interrelated pathologic process, developing at an early stage, in these hirsute subjects. In our study, the patients having raised LH/FSH ratio were 5 (8.3%), out of which only three patients had irregular menstrual cycles. The ratio was significantly different among subjects with regular and irregular menstruation and the control groups.

The results of this study provide an assessment of idiopathic hirsutism in the local population. These disorders are more frequent than previously known.[12] The importance of this finding is that a recognition of these non-PCOS disorders in hirsute women will facilitate knowledge about their pathogenesis and clinical management.

Among the limitations, we could not control the sampling of the menstrual cycle phases. We did not have an ultrasound facility available at our sampling place, hence excluding the use of ovarian morphology for diagnosis.

Therefore, we had to depend on the Rotterdam criteria for diagnosis. These limitations might have resulted in an underestimation of PCOS prevalence.[13]

CONCLUSION

The findings suggest that hirsute women are suffering from idiopathic hirsutism.

AUTHOR'S CONTRIBUTION

MSA: Conception of idea and study design
HJQ: Review critically
AB: Data collection
MQ: Drafting of article
AF: Data collection

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Original Article

STUDENT'S SATISFACTION REGARDING UNDERGRADUATE MEDICAL COLLEGE ENTRANCE EXAMINATION AND CAREER CHOICES AFTER MASTERS OF PUBLIC HEALTH DEGREE

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ABSTRACT

Backround: Each year a large number of applications are received from students in pursuance to opt for admission into a medical college. It's a career choice for the majority of the young students owing to many social or personal factors but whether this career choice is the ultimate personal choice of the respective students is the area to probe in. This study aims to explore this aspect of individual's life who are enrolled in masters of public health and to understand their satisfaction level regarding medical college entrance examination as pre-requisite for admission and also to assess their career choices after attaining currently enrolled degree.

Material and Methods: This cross-sectional study was conducted from March 2020 to August 2020. The study population is mainly comprised of post-graduate students pursuing the master of public health (MPH) in a private sector university in Peshawar, Pakistan. Using a convenient sampling method, a total of 147 students were selected. Ethical approval was sought after which the data was collected which was entered and analyzed in SPSS version 23.

Results: A total of 147 students enrolled in a public health degree program were invited to participate in this research. Among total students 52.6% of the students were registered medical practitioners and 47.4% were mainly from non-medical professions including health technology and dental technology with a majority being private employees (62.4%). The average age of students who prepared for the test for medical college admission was ≤18 years among 78.6% at the time of entry test.

Conclusion: Most of the postgraduate students enrolled in public health programs in this study setting were medical doctors. All postgraduate students had future plans for clinical practice, teaching, and research. The students were satisfied with their intermediate examination and entry test results for admission into medical colleges. However; continuing medical professions is a preferred choice among all postgraduate students studying in the university.

Key Words: Cross-sectional Study, Public Health, Career choices

INTRODUCTION

In Pakistan, a large number of students opt and apply for admissions into medical colleges each year for a medical career. Various universities offer medical degree programs specifically Bachelor of Medicine and Bachelor of Surgery (MBBS) which is offered in Pakistan in both the public and private sector.

Admission into a medical college is largely based on the performance of students during their examinations and entry test. Various studies have been conducted to assess the choices of students for selecting a medical career.[1,2] However; it is considered that admissions into medical colleges depend on the results of students which are also influenced by the personal and familial factors including parents' education and social pressures on students.[3] In Pakistan, since 1990 admission criteria in medical education has been changed from gender-based admissions to general admissions according to the merit of students. However; the pragmatic and uniformity in admissions for a medical college in past years have shown that female students have been

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performing well as compared to male students in competing for admissions in a medical college or a medical university.[4] In addition, quantitative studies assessing the success rate for qualifying admissions among medical graduates will be needed in the country. Hence, this study aimed to determine how many of the students studying public health were satisfied with the medical college entrance exam and their career prospects after getting MPH degree.

MATERIAL AND METHODS

This cross-sectional study was conducted to assess the success rate among students for qualifying admissions into medical colleges from March 2020 to August 2020. The study population is mainly comprised of post-graduate students pursuing the master of public health (MPH) at a private university in Peshawar, Pakistan. A total of 147 students (male and female) were selected who were attending MPH classes at the institute. Their verbal consent for participation in the study was sought prior. A semi-structured study questionnaire was formulated in accordance with our study objectives for data collection. It was pre-tested on 15% of the students which were excluded from the final study. The study questionnaire was self-administered and the data was collected by the principal researcher. Ethical approval was sought from the institutional review board of Sarhad Institute of Health Sciences (SIHS) Peshawar, after which the data collection was initiated. All the data was checked for its completion and accuracy. Data were cross-checked and analyzed in SPSS version 23. The descriptive and inferential results are presented as frequencies and percentages.

RESULTS

A total of 147 students enrolled in a public health degree program at a private university participated in this study. Male preponderance was higher (n = 82) as compared to female students (n = 65). Among all the students, 50.6% were unmarried and 49.4% were married. Regarding the social classification of enrolled students, a majority i.e. 63.6% claimed to belong to the low to the middle-income group and almost 36.4% belonged to the high-income group. Approximately, 64.2% had a family size of ≥5 family members including parents and grandparents; 35.8% had ≤ 5 family size. Among total students 52.6% were medical doctors who were registered medical practitioners and 47.4% were mainly from non-medical professions including allied health sciences, health technology, and dental technology. The parents of 62.4% of the respondents were private employees in comparison to parents of 37.6% who were government employees. Among all of the students who prepared for the test for medical college admission, 78.6% were equal to or less than 18 years of age at the time of entry test whereas; 21.4% were of more than 18 years of age. The qualification of 97.4% of the students at the time of admission into the medical college was pre-medical from a higher secondary school and college, whereas 2.6% were graduates at the time of admission.

Almost all of the students who were enrolled in the MPH program were employed. Among these, half of the students 48.2% (n=71) were public sector employees and 41% (n =59) were private-sector employees, 6.7% were working for a non-governmental organization and 4.1% were self-employed or were practicing in clinics. The future-plan of the majority of the students i.e. 58% was clinical profession, 23% wanted to pursue teaching as a career choice and 18.2% wanted to opt for health research as a serious career choice. Only 0.8% were anticipating their future as public health managers.

Table-1: Assessment of Satisfaction among Postgraduate Students regarding Examinations

Questions		**(%)**
Are you satisfied with the intermediate H.S.C examination results?	Yes	85.4%
	No	14.6%
Are you satisfied with the medical college entrance test/exam	Yes	49.8%
	No	51.1%
Was the process of preparing and appearing in the MCAT stressful?	Yes	77.9%
	No	22.1%

As indicated in Table-1, more than 85% of the students were found to be satisfied with the intermediate examination results and 14.6% were not satisfied with their intermediate examination results. Similarly, 73.8% of students were satisfied with the results for the entry test for medical college. 99.2% were strongly in favor of multiple-choice questions for the entrance test at undergraduate admission into medical colleges.

Table-2: Socio-demographic characteristics of respondents

Socio-demographic Characteristics		(%)
Gender	Male	55.7%
	Female	44.3%
Marital Status	Unmarried	50.6%
	Married	49.4%
Social Classification	Low – middle Income	63.6%
	High Income	36.4%
Family Size	Less than ≤ 5	35.8%
	More than ≥5	64.2%
Profession	Medical	52.6%
	Allied Health/ Health technology	47.4%
Father's Occupation	Government Service	37.6%
	Private or Self-employed	62.4%
Age at time of entry into medical college	Less than ≤18 years	78.6%
	More than ≥18 years	21.4%
Any career counseling or pre-test course before appearing for medical college test	Yes	37.1%
	No	62.9%
Qualification at time of seeking admission into medical college	Intermediate (Pre-Medical)	97.4%
	Graduation	2.6%
Type of academic institute from where qualifying examination for entry into professional school & college	Government	100%
	Private	0%
Medical and allied health sciences were your own career choice at the undergraduate level	Yes	43%
	No	57%
Reason for opting MPH Program	Academic progress	43%
	Better career prospects	57%
Future Plans After MPH	Teaching	23%
	Clinical Practice	58%
	Researcher	18.2%
	Public Health Manager	0.8%
Present Appointment Status	Public	48.2%
	Private	41.0%
	NGO	6.7%
	Self-employed	4.1%

DISCUSSION

This study was conducted to evaluate the students' satisfaction regarding undergraduate medical college entrance exam and their career choices after attaining Masters of Public Health Degree. In Pakistan, the students who have passed the intermediate exam (pre-medical) appear in the medical college entrance exam as a pre-requisite for admission into all medical and dental colleges across the country. This study inducted the postgraduate students enrolled in MPH program. 55.7% of the participants were males and 44.3% were female which slightly corresponds to a study in which there where 56% were female and 44% were males.[5] 77.9% believed that both preparing and appearing for MCAT was stressful which was inconsistent with a study published in 2012 where around 81% students considered undergraduate medical and health sciences entrance exam as stressful.[6]

In this study 37.1% of students responded to had taken pre-test courses before appearing for the actual medical college entrance exam whereas 62.9% didn't take any career counseling and pre-test courses. In another study, 31% of students had taken the university medical admission course prior to seeking actual test.[7] Owing to the circumstance in Pakistan, the pre-test courses offered by various private academies have high admission charges and even if students at the FSC level join these academies, it's not a guarantee to secure a place in actual tests.

In a study conducted in Pakistan, 26% of the students had joined the medical profession according to the will of their parents or guardians whereas in this specific study 57% of respondents mentioned it to be the choice of someone else for them.[8] Opting for a specific medical profession on your own will helps the individual to get more motivated to excel in that profession. Although the results of a qualitative study conducted in Malaysia suggested that student's motivation can change over the course of time so are their career choices as 52.6% of the participants in our study directly belonged to the medical profession however, all ended up being

enrolled in MPH degree as a post-graduate option so the choices of students do tend to change.[9] A systematic review to probe into the factor which motivates the students to make medical a career choice revealed that in low- and middle-income counties it's also the societal factors whether parents or peer pressure that decided for career.[10-12]

In this study 52.6% of participants were medical doctors whereas 47.4% were from allied health sciences. In another study, three-quarters of the respondents were not doctors but they opted for the master of public health degree to seek better opportunities to work in the public health domain.[8] This study observed that 18.2% of the participants wanted to opt for research as a potential career choice after attaining the MPH degree which is comparable to the study conducted in India, research was identified as a potential career opportunity after MPH degree.[13] Similarly other studies also reflected benefit and diversity in the future career prospects after MPH.[14,15] Public health, undoubtedly is key to robust initiatives for improvement in the quality of life.[16] Regardless of the health profession any individual has at the time of attaining a master of public health degree, the career dynamics are diverse owing to the domains and diversity of public health in Pakistan. Individuals get opportunities to opt for teaching, research, or administrative positions after attaining the respective degree. Since this study was unique in being retrospective regarding recollecting their events from the intermediate level, the results would have strengthened if we could gather data regarding their intermediate marks and medical college entrance examination scores but since the scope of this study was not that much diverse, it can give a way forward to future studies based on the scores and their reflection in terms of student satisfaction to validate the perception regarding such entrances examination.

CONCLUSION

The study findings conclude that although the majority of the students were satisfied with the undergraduate entrance test format and their results, their career choices after attaining a master's of public health degree were diverse. This enhances the need for student counseling at both undergraduate and postgraduate levels so that they should exactly determine the value of getting into that specific degree and its effective utilization for their career progression.

AUTHOR'S CONTRIBUTION

SA: Supervisor of study and study design
SAK: Data collection
SA: Critically review
SAK: Drafting article

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Original Article

ANTERIOR KNEE PAIN SIX MONTHS AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

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ABSTRACT

Background: Pain at the anterior part of the knee is one of the major complications besides others that are associated with anterior cruciate ligament (ACL) reconstruction. Prevalence of anterior knee pain varies with the site of graft chosen for ACL reconstruction, with high prevalence when bone-patellar tendon-bone (BPTB) is used as autograft. The objective of the study was to determine the number of patients with anterior knee pain associated with ACL reconstruction after six months of surgery.

Material and methods: It was a cross-sectional study in which 81 patients undergoing ACL reconstruction were included as per inclusion and exclusion criteria. All patients included in the study were male with the same baseline characteristics, patients were assessed using an anterior knee pain scale (AKPS) six months of reconstruction surgery.

Results: Mean age of patients was 30.8 years, Range 17 years to 60 years out of 81. Patients with no history of pain were 35 (43.2%). The pain was occasionally severe in 28 (34.6%) patients.

Conclusion: Almost 60% of the cases post ACL reconstruction with bone-patellar tendon graft complained of anterior knee pain of mild to moderate severity even after six months of re-construction according to the anterior knee pain scale (AKPS).

Key Words: Anterior Cruciate Ligament, Pain, Patients

INTRODUCTION

Ligaments provide static as well as dynamic stability across every joint of the human skeleton. The anterior cruciate ligament has a stabilizing effect at the knee joint, preventing anterior translocation of the tibia. Damage as a result of trauma to this ligament commonly results in instability and functional loss at the knee joint. Conservative management and surgical reconstruction of the anterior cruciate ligament is usually done to regain its normal function. Reasons behind anterior knee pain after ACL reconstructive surgery are chronic ligamentous laxity, femoral and tibia tunnel malposition, mal-tracking, and failure of fixation; They play an important role as main causes for knee pain leading to failure of ACL reconstruction.[1]

Intramedullary nailing of the tibia is another common cause of anterior knee pain, a major complication of this open surgical procedure. Dissection of the patellar tendon and its sheath during nailing is thought to be a contributing cause of chronic anterior knee pain; other causes may include athletic activities, falls, automobile accidents, and hyperlaxity of the knee joint. Similarly, shortening of quadriceps with impaired length-tension relationship show decreased motor unit recruitment and loss of significant patellar stability which had a close association with new cases of patellofemoral pain. The latter four parameters play a dominant role in generating anterior knee pain and are risk factors for this syndrome.[2]

Prevalence of anterior knee pain after ACL reconstruction is 30% when the BPTB is used

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as autograft and 48% when the hamstrings tendon is used as a graft.[3] Reconstruction surgery of anterior cruciate ligament (ACL) is common in the adolescent. Time taken between ACL rupture and surgical reconstruction is related to concurrent meniscal tear incidence and possibly tear pattern. The administration of Nonsteroidal Anti-inflammatory Drugs (NSAIDs) to patients undergoing anterior cruciate ligament reconstruction surgery is subject to controversy owing to the impairment it causes in tissue healing and clinical outcomes.[4]

It also has been suggested that anterior knee pain is related to the type of graft chosen for reconstructive surgery. Mainly two graft options are available i.e. hamstring tendon (HT) and bone BPTB. Anterior knee pain is more common after ACL reconstruction using (BPTB) than by using Hamstring Tendon (HT). Post-operative complications of ACL reconstruction include prolonged knee stiffness, limitation of complete extension, and pain at the anterior section of the knee. Emphasis on getting complete knee extension (terminal knee extension) on the first postoperative day and weight-bearing training from the very first day according to the patient's tolerance decrease complications to some extent.

The objective of the study was to explore the number of patients who complain of anterior knee pain after bone tendon-bone graft open ACL reconstruction so that early measures could be taken to reduce the development of this complication and improve patient's performance.

To describe the percentage of patients with anterior knee pain associated with open ACL reconstruction with bone-patellar tendon-bone graft, six months post-operatively.

MATERIAL AND METHODS

The non-probability convenience sampling technique was used for this cross-sectional study carried out at Ghurki Trust Teaching Hospital Lahore. The sample size was 81 with 30% prevalence (p)< 0.01 precision (d) and 95% confidence interval (1-a). Patients were distributed into age groups. The frequency of patients was 31 for 17-25 age group 15 for 26-35 age group and 24 for 36-45-year age group. The highest (31) frequency lies in the 17-25 age group.

The patients were recruited as per the inclusion criteria. Subjects with 6 months after ACL reconstruction surgery with bone-patellar tendon-bone graft. Patients having neurological deficits, vascular problems, active neoplasm, and bone tumors were excluded from the study. Assessment Tool: Anterior Knee Pain Scale (AKPS) was used with test-retest reliability AKPS-0.95 with CI=95%.

Permission from the institutional ethical committee was obtained to carry out the study. The duration study was only six months.

RESULTS

According to the anterior knee pain scale, out of 81 patients, no one had severe anterior knee pain. 16 (19.8%) patients had moderate anterior knee pain and 30 (37%) patients had mild anterior knee pain. The frequency of patients without anterior knee pain was 35 (43.2%). (Table-1, Figure-1)

Table-1. Frequency of Knee pain according to AKPS.

Anterior Knee Pain Scale	Frequency	Percentage
Severe Knee pain (0-30)	0	0.00
Moderate Knee Pain (31-60)	16	19.8
Mild Knee Pain (61-80)	30	37.0
No Knee Pain (81-95)	35	43.2
Total	81	100.0

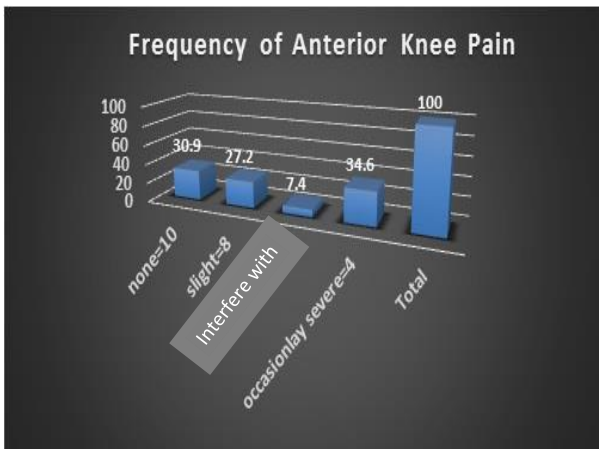

Figure 1. Out of 81 patients, 30.9% had no anterior knee pain, 27.2% patients had slight anterior knee pain, 7.4% patients had pain interfering with sleep and 34.6% had occasionally severe anterior knee pain.

DISCUSSION

Important satisfactory results were found in the present study, where no pain was found in 35 subjects (43.2%). Among the patients complaining of pain, no patient complains of severe pain, whereas 8 subjects reported pain at rest, or with activities varying from mild to strenuous activities of daily living. Studies upon anterior knee pain state that incomplete or non-fulfillment of expectations to manage pain after major surgeries result in anxiety leading to more pain, but measures are taken at the earliest to make it possible to reduce anxiety among patients. Involved interventions are ROM exercises, regaining terminal knee extension.[5]

The anterior cruciate ligament has a stabilizing effect at the knee joint, preventing anterior translocation of Tibia. Damage as a result of trauma to this ligament commonly results in instability and functional loss at the knee joint. Injury to the anterior cruciate ligament most commonly occurs during athletic activities and automobile accidents. Young adults most commonly undergo the procedure of anterior cruciate ligament reconstruction.

Studies have also shown that stabilization training of not only knee but hip and core stabilization exercises are also important to post knee joint surgeries. The conventional treatment protocol that involves avoiding achieving terminal knee extension is not supported by studies claiming it has no destabilizing effect on operated knee. Supporting the idea that early intervention must be taken to meet the outcomes after the surgical procedure. Joint osteoarthritis can occur due to pain which can categories into three forms mild, moderate, severe, and biomechanical changes leading to impaired arthrokinematics.[8] Anterior Tibia translation was found similar for the reconstructed and sound limb however, the reconstructed limb was also more adducted. Although small differences were found, but they were consistent in all subjects. At 2 years post-ACL-reconstruction (injured) knee showed greater medial compartment mobility because of pivoting about a more on lateral KCOR (p= .03) than the contralateral knee.[9] Risk factors for graft failure include returning to a high activity level post ACL reconstruction and using an allograft.[10]

A hypothesis has proposed that the mechanism for ACL injury is valgus loading as well as lateral compression generating internal rotation motion and anterior translation of tibia, due to the joint symmetry, causing ACL damage.[11] Knee motion and knee loading during a landing phase are predictors of anterior cruciate ligament injury risk in female athletes.[12] The intensity of pain was not associated with either operative technique, any adjoining lesions, or methods used to treat them. Neither surgical technique nor concomitant lesions and methods used to treat them.[13] Knee flexor and extensor peak torque values were found greater in subjects undergoing postoperative rehabilitation in their reconstructed limbs in comparison to parents treated by usual care.[14] Physical training with stabilization training plays a vital role in the early rehabilitation of patients post ACL reconstruction surgery. The role of

Kinesio taping is important in improving swelling, night pain, and flexion range of motion.[15]

Van Jonbergen et al. have concluded in a systematic review that re-construction surgery can done when indicated without any harmful outcome associated with it. Various studies were included that compared pain between inpatients and outpatients after one to two years of ACL reconstruction surgery by using the Visual Analogue Scale (VAS).[6]

This study suggests a greater rate of anterior knee pain with advancing age than adolescent patients, with greater frequency of limp, swelling, atrophy, and muscle imbalance specifically imbalance between vastalis medialis and lateralis. Symptomatic knee flexion contractures had been reported after ACL reconstruction. Based on these observations, it can be deduced anterior knee pain after ACL reconstruction is closely associated with persistent knee flexion contracture. More specifically, anterior knee symptoms seem particularly prevalent in patients who fail to regain full hyperextension equal to the contralateral knee. Different variables that have been found with respect to the prevalence of AKP include knee-specific characteristics, prosthetic design, surgical technique, adjustment of the patella baja and the instance at which assessment has been done.[7]

Studies have shown that incorrect biomechanics, muscle imbalance (impaired length-tension relationship) patella baja cause osteoarthritis of the knee as well as hip joint with deformities like kyphosis.[5]

The limitation of the study was that this study was done in a single hospital setting (Ghurki Trust Teaching Hospital, Lahore, Pakistan) and the sample size of the study was too small because the study time duration was only six months.

The recommendation was that the study can be improved by increasing the sample size and by choosing different hospital settings.

CONCLUSION

Almost 60% of the cases after 6 months of ACL reconstruction with bone-patellar bone graft complain of mild to moderates pain in the anterior section of the knee according to the anterior knee pain scale (AKPS).

AUTHORS CONTRIBUTION

MA: Drafting of article, Data Analysis
NJ: Drafting of Article, Collection and assembly of data
MWA: Critical Appraisal of article
MMA: Critical appraisal and final approval of article

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Review Article

PERFORMING SAFE GI ENDOSCOPY AMID COVID-19 PANDEMIC IN PAKISTAN

Shahzad Latif[1], Hafiza Bushra Saleem[2], Raja Omer[3], Wafa Qaiser[4], Tariq Waseem[5]

ABSTRACT

Coronavirus disease (COVID-19) is being declared as a global pandemic by the World Health Organization after its emergence from China. Body secretions including respiratory aerosols and feces and environmental surfaces exposed to these secretions are listed as the main cause of human-to-human transmission. Previous reports have strongly suggested that a significant number (29%) of COVID-19 patients were healthcare workers in the medical facilities. It is inevitable to avoid exposure to either respiratory or gastrointestinal fluids from patients during endoscopy. This presents a great risk of the infecting virus to skilled medical professionals. Various endoscopy societies and the leading organization has published a suite of recommendations based on the expert's opinion and experiences of handling the pandemic. However, each society has also greatly emphasized to develop appropriate contingency plan on management and preventive measures based on specific resources and COVID-19 patients at each endoscopic center. Since the COVID-19 cases are continuing to rise, we aim to review the literature and compile a set of recommendations implacable in Pakistan to limit the spread of COVID-19 in endoscopic facilities. Lack of awareness, poor compliance, socio-economic factors, limitations of national health resources, and lesser resilience in the health system are key challenges. However, designing a COVID-19 response management system, preparedness and use of appropriate Personal Protective Equipment (PPE) can ensure zero transmission of the contagious pathogen-associated outbreak and hygienic endoscopy services without subjecting patients and staff to undue health hazards.

Key Words: COVID-19, Pandemic, Endoscopy

INTRODUCTION

Coronavirus disease (COVID-19), caused by new coronavirus of SARS-CoV-2, initially emerged as an epidemic in Wuhan, China and rapidly spread all over Asia and the World Health Organization (WHO) declared COVID-19 as a global pandemic on 11 March 2020.[1] Human-to-human transmission appears to occur through secretions of respiratory systems including aerosols and feces, and contaminated environmental surfaces.[2,3]

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It has been suggested that both symptomatic and asymptomatic individuals can be a source of transmission.[4,5] Likewise, SARS-CoV-2 can survive in confined public spaces i.e., toilets, elevators corridors, and doorknobs.[6] A recent study revealed that the source of the vast majority of COVID-19 patients remained untraced primarily due to community transmission suggesting a higher number of cases than reported.[7] Thus, the risk of contracting the infection is higher than anticipated particularly to healthcare workers. It is evident from the earliest reports from Wuhan province where a significant number (29%) of COVID-19 patients were healthcare workers in the medical facilities on the premises.[8] The spread of the virus globally suggests that the earliest measures to contain the virus were insufficient regionally as well as globally. Lack of coordinated systems, misapprehension of the mode of transmission of the virus and poor resilience

in the medical system against infectious diseases particularly in developing countries are key bottlenecks to contain the virus. It is well anticipated that an asymptomatic individual visiting a medical facility could potentially be a source of infection to healthcare workers. Therefore, it remains uncertain whether the spread of the virus in healthcare workers was due to direct contact with the patients or associated with exposure to fomites due to inadequate use of Personal Protective Equipment (PPE).

Medical procedures such as endoscopy where exposure to fluids/droplets either from the respiratory or gastrointestinal system of patients is inevitable present a great risk of the contracting virus to skilled medical professionals. Although, no evidence has suggested so far positive insufflation during routine endoscopic procedures could present a risk of generating aerosol, thus higher risk of SARS-CoV-2 transmission. Healthcare workers involved in endoscopic procedures, therefore, are facing immense hazards during the COVID-19 pandemic as it disseminates mainly through direct contact or aerosol droplets.[1] Thus, adequate protection of healthcare workers is critical amid the COVID-19 pandemic.

There has also been a great deal of literature published on safe work procedures in healthcare facilities. The World Endoscopy Organization has recently published a series of recommendations to prevent infection and control in digestive endoscopy procedures after reviewing cases in China.[9] In addition, the American College of Gastroenterology and the British Society of Gastroenterology, and the Asian Pacific Society for Digestive Endoscopy (APSDE) developed their position papers based on expert's opinions and current experiences in handling the pandemic under specific conditions and resources. On the contrary, each society has emphasized that endoscopic centers are required to develop their own contingency plan on management and preventive measures based on specific resources and the number of in-coming COVID-19 patients. This will help to contain the virus from the spread and ensure safe and high-quality endoscopy services without putting patients and staff to undue health hazards. Since the number of COVID-19 cases continuing to rise, we aim to review the literature published for safe work procedures during endoscopic procedures and compile a set of recommendations presenting practical aspects implacable in Pakistan to limit the transmission of COVID-19 in the endoscopy units.

Risk Assessment

Each healthcare facility should delineate resources to investigate the risk of a patient with suspect or confirmed cases of COVID-19 for screening and risk-stratified before the arrangement of an endoscopic procedure.

The WHO characterized COVID-19 confirmed patients with laboratory investigations of infection, irrespective of clinical signs and symptoms[10] while a suspected case, for whom testing in inclusive, based on three criteria: (1) patient having acute respiratory symptoms with no history of travel or residence in the country reporting community transmission of COVID-19 the past 14 days before the onset of symptom; (2) patients with acute respiratory symptoms having in contact with a confirmed or suspect case of COVID-19 in the past 14 days before the onset of symptoms and (3) patients required hospital admission with severe acute respiratory infection having no other clinical cause required for COVID-19.[10]

The APSDE has emphasized deferring elective endoscopic procedures (Table 1) until the COVID-19 pandemic is over. This will help to spare surgical facilities to handle an anticipated large number of suspected or confirmed cases of COVID- 19 while limiting the risk of transmission to healthcare providers and between patients.[11,12] It will also allow the time required for the necessary education and training of healthcare providers at endoscopic centers. A retrospective case study from Iran reported the death of three patients out of four after contracting COVID-19 infection at elective surgery.[13]

Transmissions modes of SARS-CoV-2 during endoscopy

The characteristics of the SARS-CoV-2 virus and the potential transmission method recognized to date make endoscopic procedures a risk of contracting infections. Nearly half of the patients diagnosed with COVID-19 exhibited GI symptoms including anorexia (83.8%), diarrhea (29.3%), and vomiting (0.8%) with an increasing trend of severity with the disease progression.[14] In addition, reports from the SARS epidemics suggested the presence of coronavirus in stool samples and intestinal biopsy samples.[15] Evidence has been provided recently that COVID-19 can be present in the oral cavity and fecal samples of infected patients.[3,16-18] This suggests an association of the GI system as target incubation sites for the virus in the body and thus the source of infection. Potential modes of transmission of SARS-CoV-2 recognized include (I) person-to-person contact, (II) respiratory droplets, (III) aerosols, and (IV) body fluids and previously contaminated surfaces.[2,14] The virus is detected in the blood and other secretions thus additional care is required in handling samples. The risk of fecal contamination is not known yet but SARS-CoV-2 has been detected in the faecal samples of patients regardless of the symptoms.[9,17,18] Thus it remains plausible that the virus may sustain even with a negative result of respiratory tract sampling and present a risk through aerosolization and fecal-oral route of contamination.[19] Evidence has been reported in a recent study demonstrating the persistence of viral RNA up to 47 days in faecal samples after the onset of the symptoms.[20] Endoscopes are often exposed to gut flora a vector of the infection, thus pose a risk to endoscopists, nurses, and other assisting staff. A study conducted in Hong Kong during the SARS outbreak reported that the risk of infection is highest for healthcare assistants (8%), followed by physicians (5%), and nurses (4%).[21] This study and modeling work presented the Imperial College COVID-19 response team, which has emphasized the suppression policy comprising of strict isolation, use of appropriate PPE, and other infection control measures can significantly reduce infection and mortality.[11,21] The Centers for Disease Control and Prevention (CDC) has recommended the use of a separate bathroom for infected patients as the virus was detected in feces. Therefore, limiting oral-fecal transmission and adopting appropriate measures is critical to limit the spread of the virus through these routes. It is widely suggested that the individual with recent travel history to COVID-19–affected areas should isolate in self-quarantine for 14 days regardless of any apparent symptoms of the disease to eliminate the risk of transmission.

Our Challenge

Lack of awareness, poor compliance to control measures, and various other socio-economic factors possibly contribute to the increasing number of cases in developing countries like Pakistan. On the other hand, an efficient health system aims to achieve zero viral transmission among healthcare workers providing essential services to the patients. This becomes more important for a health system with less resilience and overwhelming burden and lack of sufficient skilled human resources. GI community in Pakistan presents such skilled human resources at risk and there is a dearth to prevent exposure during any endoscopic procedure. Henceforth, it requires to develop a checklist of standard operating procedures based on available resources at the medical facility. The use of appropriate quality PPE and their disposal remain paramount to prevent the spread of the virus. We present some general measures required to be considered while formulating an inventory of the standard operating procedures.

Standard Operating Procedures: Management

1. Training of the essential personals associated with endoscopy i.e., endoscopists and other healthcare providers on the use of PPE to ensure the limited risk of viral spread during endoscopy is key to effective and

resilient institutional strategy to prevent the spread of the virus.[22-24] It warrants that staff understand their responsibilities and are held accountable in case of any unanticipated circumstances. Following a standard hand hygiene protocol before and after each procedure with appropriate disinfectant (62-71 % ethanol, 2% glutaraldehyde, and 0.1–0.5% sodium hypochlorite) can significantly reduce virus load within 1 min of exposure time.[25] We suggest the risk stratification derived decision making of the use of PPE according to (Table 1).

2. Preparedness and a robust system of managing staff is an important part of performing endoscopic procedures during the COVID-19 to attain zero transmission during the pandemic. The procedure should be ideally conducted in a negatively pressured room if available.[26]

3. Establishment of a rapid communication mechanism using various information technology tools is important, so updated information of patients and equipment is available for staff across the entire facility.

4. Encouraging regular feedback on the delivery of the response system and updates on the recent development of research outcomes among administrators, infectious control team, doctors, and paramedics to ensure unified efforts exerted to prevent the transmission.

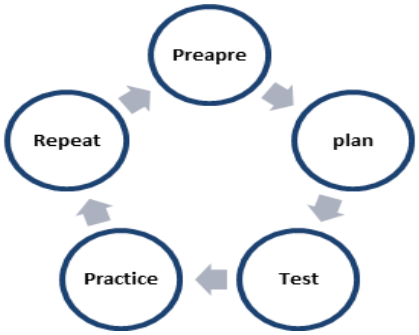

Figure 1. Presents essential elements of standard operating procedures for effective virus transmission control strategy

Preparation

1. Pandemic requires establishing a separate reception area to collect initial history and assess the risk of COVID-19 infection. This could follow directing the patient to the appropriate section of the facility ensuring a sitting plan of 6ft distance between patients and hygienic procedures to warrant zero contamination risk in the waiting area. Establish a separate food area in the facility to ensure maximum hygiene.

2. Preventing staff to staff transmission is very critical and requires safe workflows including individual stations with minimum sharing of the equipment such as a computer, phone, and stationery. It also involves wearing appropriate PPE, disinfecting workstations, and associated equipment during the transition of the staff after work hours with recommended viricides using the correct dosage.

Figure 2. Visual presentation of the use of PPE for general patients and handling of suspected/confirmed cases of COVID-19

3. Developing and disseminating self-explanatory pandemic workflow enlisting clear tiers of job descriptions. For instance, effectively dividing clinical personnel into multiple teams at well-defined intervals of service delivery with the flexibility of a backup plan, in case a member of the team is unavailable or requires quarantine.

Indications for procedures

Indications for critical GI procedures include managing upper GI bleeding, acute cholangitis, obstructions associated with a foreign body.[9] Cancer patients that require preliminary diagnosis, biopsy, staging, palliation of biliary and luminal obstruction could be considered urgent depending upon clinical evaluations. Other non-essential procedure (Table 2) could be rescheduled depending upon the availability of resources and allowing the provision of medical attention and institutional resources for the terminally ill patients. This could additionally prevent the potential risk of contamination, particularly from asymptomatic patients.

Endoscopic procedures require a short physical distance between patients and healthcare providers. It has been previously suggested in 2003 during the SARS outbreak that aerosol droplets from infected patients could reach two meters or more from the source.[27]

Table-1: Type of endoscopy procedures and appropriate PPE[1] required (regular or specialled), manpower and frequency of gown down[26]

Procedure	AGP[2]	Regular PPE for non-suspected/test negative cases	Specialled PPE for high risk/confirmed patients	Endoscopist manpower	Endoscopy nurses manpower	Frequency of gown down
Colonoscopy	To be determined	Regular mask or N95, Gloves, Isolation gown, regular procedural facility	N95, glovers, gown, safety goggles or face shield, negatively pressurised room	1 (at specialist level	2	Gloves and mask: Use new for each procedure, gown as required after contamination
ERCP[3]	To be determined	Gloves Surgical mask or N95, Blue isolation gown, and gloves.	N95, glovers, gown, safety goggles or face shield, negatively pressurised room with ample space and X-ray shielding	1 (at specialist level)	2	Gloves and mask: Use new for each procedure, gown as required after contamination
Bronchoscopy	Yes	Gloves, N95 mask, safety gown, safety glasses of the face shield, negatively pressurised room	N95, Blue isolation gown gloves. Safety glasses or face shield, negatively pressurised room		2	Gloves and mask: Use new for each procedure, gown as required after contamination

[1]Personal Protective Equipment. [2]Aerosol Generating Procedure; [3]Endoscopic Retrograde Cholangiopancreatography[26]

Table 2 enlists the classification of urgent, semi-urgent, and elective endoscopic procedures. Elective procedures could be deferred in case of an outbreak based on cases to case need and indications of patients and decision made by clinicians.[26]

Urgent endoscopy	**Semi-urgent endoscopy (to be discussed on a case by case basis)**	**Elective endoscopy (deferred until further notice)**
Assessing GI bleeding caused by acute gastrointestinal and ulcers, biliary sepsis, stent due to foreign body and other obstruction, GI access for urgent feeding	Treatment of GI neoplasia (EMR[1]/ ESD[2]), assessing possible cancer, bleeding, small bowel enteroscopy for the occult, ERCP[3] for hepatobiliary pancreatic cancers	Regular endoscopic procedures for diagnosis and follow-ups, ERCP or other treatments of non-cancerous conditions, asymptomatic stones; chronic pancreatitis; insertion/replacing metal stent, check-ups for ampullectomy, diagnostic procedure for benign cancer, bariatric, GORD[4],
[1]Endoscopic Mucosal Resection, [2]Endoscopic Submucosal Dissection, [3]Endoscopic Retrograde Cholangiopancreatography, [4]Gastro-Oesophageal Reflux Disease		

Recommended practices in case of marked community spread of COVID-19

1. Establish a screening station at the entrance of the facility and require every individual including staff to get screened for body temperature before commencing their work. The vulnerable staff member with impending conditions shall be prevented from work.
2. CDC mitigation strategies in case of substantial community transmission require all staff to wear PPE while in the facility.[28] A high viral load in the upper respiratory tract poses an important risk of viral transmission particularly from asymptomatic persons.[29] Persistence of viable viral load on the contaminated surfaces for a prolonged period suggests that all staff must wear PPE at all times at work.[5]
3. Staff require social distancing while working at individual workstations with minimum risk of cross-contamination. Restrict the use of shared facilities, equipment, and encourage regular disinfection of the area.
4. Reduce the number of staff and paramedics in the endoscopy suite to the essential numbers while off-duty staff can stay home as much as possible. Limit/restrict the movement of support personnel of patients in the facility.
5. Use the data lodger to record the visitor and healthcare workers in the facility with their contact numbers. This record may facilitate to advise self-quarantine in case of exposure to the COVID-19 patient.
6. Staff required for endoscopy must use scrubs provided at the facility and use endoscopy shoes and gear should remain in the hospital in the preparation room. Regular disinfection of gear and disposal of used material should be performed and recorded with the mention of the date, time, and disinfectant.
7. The COVID-19 screening guidelines continue to evolve but symptoms resembling such as fever and/or symptoms of acute respiratory illness should be assessed at the time of admission. Potential contact of healthcare workers with a suspected or laboratory-confirmed COVID-19 should be quarantined.
8. The availability of testing kits for COVID-19 at the endoscopy facility may facilitate a more accurate stratification of the potential risk of contamination.

Before the procedure:

Outpatients

1. Risk assessment by screening the patient with symptoms, signs, and exposure to COVID-19 positive case or travel history to effect area. Monitor their temperature at the facility to risk stratify.
2. In case of a pandemic, it is imperative to test suspected patients for COVID-19 using RT-PCR[30] and decide appropriate at the receival of the results if possible.
3. Restrict the movement of the patient in the facility while waiting for the procedure to minimize facility contamination.

In-patients

1. Inquire about symptoms for any suspected COVID-19 coming to endoscopy units and triage appropriately.
2. Prior to endoscopic procedures, all patients should be subjected to COVID-19 testing using real time-PCR[30] and wait until results are received if possible.
3. All patients should receive PCR-based testing for active COVID-19 infection at least 48 hours prior to the procedure.

Disinfection protocol

Disinfect the reusable medical equipment (RME) as no evidence has been suggested otherwise. It is important to note that the highest risk of contamination is accounted for pre-clearing of the endoscope due to air and water splashes. Thus, it remains imperative to switch off the processor while replacing the credit card button from the air/water button. SARS-CoV-2 is sensitive to all frequently employed disinfectants for example; organic solvents and chlorine-based solutions. The CDC provides a comprehensive list of standard operating procedures for cleaning and disinfection. Strict compliance with personnel hygiene in the unit remains fundamental that could be achieved after appropriate training, practices, and maintaining a regular record of proficient quality control. Staff must adhere to the adopted protocols and collaborate across the facility so all mechanisms of containing the virus are functioning in synergy. In conclusion, guidance and key recommendation provided here are based on rationally developed practical experience, careful observations, and literature published previously. However, it is subjected to the realization that our understanding of SARS-CoV-2 is rapidly evolving in the light of recent research.

Conflict of Interest

The authors declare no conflict of interest.

AUTHOR'S CONTRIBUTION

SL: Conception of idea and study design
HBS: Data collection
RO: Drafting article
WQ: Data collection
TW: Critically review

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Case Report

A YOUNG GIRL WITH ACUTE IMMUNE THROMBOCYTOPENIC PURPURA

Ayesha Choudhry[1], Arsham Najeeb[2], Ehsan ul Haq[3], Agha Shabbir Ali[4]

ABSTRACT

Immune thrombocytopenic purpura (ITP) is an immune-mediated acquired disease in both adults and children. It is characterized by transient or persistent reductions in the platelet count. We report a case of ITP presenting with intermittent fever and oral hemorrhagic symptoms. The patient was a 9-year-old girl with no significant past medical history. She presented with sudden onset gum bleeding and hemorrhagic bullae on the buccal mucosa. During night pinpoint purple spots (petechiae) appeared on the body mainly, on the lower legs. Laboratory tests revealed severe thrombocytopenia with a platelet count as low as 2000/mm^3. Under a provisional diagnosis of Acute ITP, she was treated with 1 mega unit platelets transfusion and high dose immunoglobulin therapy. Her platelets rapidly increased, and no bleeding complications were reported.

Key Words: Gingiva, Hematoma, Hemorrhage, Purpura

INTRODUCTION

Immune thrombocytopenic purpura (ITP) is an acquired hematological disorder that is developed due to the production of auto-antibodies against platelets leading to isolated thrombocytopenia, in the absence of other causes of thrombocytopenia such as drugs, infections, malignancy, or other autoimmune diseases.[1,2] ITP commonly affects children between one and seven years of age. Parents are much concerned as they see such symptoms first time in children. Severe life-threatening bleeding is rare (0.2–0.9%).[3,4] Childhood Primary ITP usually is a self-limiting disease, with or without treatment. Complete remission occurs within six months after diagnosis, commonly within 6–12 weeks, in the majority of children. However, 20–30% of children continue to have persistent low platelets count with bleeding symptoms beyond six months after the diagnosis.[5,6]

CASE DESCRIPTION

A 9 years old girl student of 3rd class with no significant past medical history presented in peads emergency at Farooq Hospital on 21-08-2020 with a history of intermittent fever, gingival bleeding for the last 4 days. She was taking some oral medicine from a local practitioner for this complaint without any improvement. A day before admission, she developed pinpoint reddish-purple spots (petechiae) more marked on the lower limbs (Figure-1) and face, than gum bleeding was persistent and was getting difficult to control thus she was brought to peads emergency. There was no personal history of any bleeding problem and her family history was also insignificant regarding bleeding disorder or coagulopathy.

Examination at the time of admission revealed a young girl looking comfortable regardless of multiple new and old purpuric spots on the face and both lower limbs. She had stable vital signs including blood pressure. Her weight was 20kg with 130cm height and was at 25th centile for her age.

There was no lymphadenopathy and the liver, the spleen was not palpably enlarged. The rest of the systemic examination was unremarkable.

First Complete blood count revealed Hb 11.9 g/dl, TLC 5.3/mm^3, neutro 37%, lympho 54%, and severe thrombocytopenia with

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platelet count 2000/mm^3. X-ray chest and ultrasound abdomen were normal. Blood culture revealed no growth.

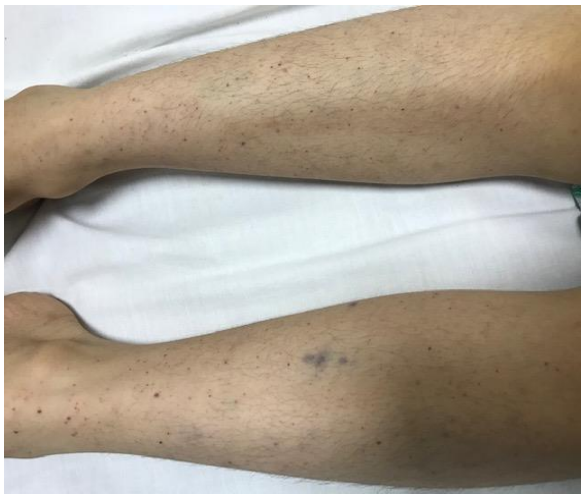

Figure-1. Multiple bruises and a petechial rash over both shins

Differential diagnoses before investigation included ITP, aplastic anemia, acute leukemia, and dengue fever. The dental consultant's opinion was also taken on this case. Considering the clinical behavior, absence of lymphadenopathy, and hepatosplenomegaly with isolated thrombocytopenia, the diagnosis of immune thrombocytopenia was made.

The patient was initially managed by IV fluids and oral antibiotics for stomatitis and gum bleeding. Due to the critically low platelet count (2000/mm^3), 1 Mega unit of platelets was transfused. We planned to treat her with immunoglobulin IgG as immunosuppressive therapy. The total dose decided was 2 gm/kg. Twenty (20) gm IVIG was given to the patient on two consecutive days. Clinically she improved within 24 hours as no new bruise or purpuric spot appeared after the first IgG infusion. CBC report showed improvement in platelet count within 48 hours.

The patient was discharged on the 4th day when she was clinically stable and platelet count was >70,000/mm^3. She was to follow up after 3 days.

After one week on her 1st follow-up, bruising completely disappeared and platelet count was 222,000/mm^3.

DISCUSSION

Idiopathic (autoimmune) thrombocytopenic purpura (ITP) is the most common cause of thrombocytopenia in children. Peak age is 2-5 years but also seen in adolescents as well as in younger children. The exact cause of ITP is not known but in 60-70% of babies, there is a history of viral throat infection 1-2 weeks ago. Antibodies produced against these viruses destroy host platelets as well. These antibodies fix on surfaces of platelets and make them easily sequestered in the spleen. Thus the number of platelets decreases (thrombocytopenia) which is responsible for the bleeding manifestation of the disease.[1]

Cutaneous bleeding i.e. bruises, purpura, and hematomas are common clinical manifestations in the baby with ITP who is otherwise well looking. Some children do have bleeding from mucous membranes e.g. epistaxis, gum bleeding, or hematuria. Fever, bone pains, lymphadenopathy, and splenomegaly are not regular features of ITP in children.[1,3]

ITP needs to be differentiated from other causes of thrombocytopenia in children e.g aplastic anemia, acute leukemia, and inherited platelet disorders. Most babies with these disorders are sick-looking and have lymph node enlargement or splenomegaly and bone pain.

In ITP CBC depicts reduced platelets count while red cell and white cell number is normal. Anti-platelets antibodies are on the rise but are generally not required in clinical practice. Bone marrow examination is subjected to the clinical experience of the pediatrician. If any clinical association creates doubt of an alternate diagnosis e.g acute leukemia then he may ask for bone marrow biopsy.

Two issues are important in the management of ITP in children

1. When to treat
2. Which drug to be used in the treatment of these babies.

ITP in children is a self-limiting disease in most of cases.[5] But the number of platelets count and site of bleeding decide the timing of treatment in many cases. Platelets count <

10,000/mm^3 and bleeding from mucous membranes e.g. nose, gums or hematuria also are indications of platelet transfusion. In this case, platelets dropped to 2000/mm^3 and she was bleeding from oral mucosa at the time of admission. It necessitated platelet transfusion and IgG therapy.

Steroids, immunoglobulins; IgG, IgD, and other Immunosuppressive drugs are used in acute ITP. These three drugs are taken as first-line drugs in the management of ITP. IgG is the first choice in children and steroids are used in adults. Oral prednisolone 2-4 mg/kg/day for 2 to 3 weeks is commonly used. This therapy is cheap and easy but needs bone marrow biopsy before therapy. IgG immunoglobulin is costly and associated with the risk of aseptic meningitis. In our case report platelets, the number started rising within 24 hours. Clinically, bleeding manifestations were improved within 48 hours.[2,3]

Anti D therapy is also cheap and of short duration but associated with risk of anemia. Thus Hb should be adequate before this therapy and is only carried out in positive blood group patients. Monitoring of response to therapy is carried out by the rise in platelets number. Complete response (CR) is platelets count more than 100,000/mm^3. Response (R) means a platelet count of 30,000/mm^3 on two occasions in a week. In both conditions, clinical symptoms should also disappear.[7,8]

AUTHOR'S CONTRIBUTION

AC: Collection of data
AN: Writing of article
EH: Critical review
ASA: Supervisor of the study

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