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ORIGINAL ARTICLE OPEN ACCESS

Thyroid Function Tests in Ankylosing Spondylitis Patients on Anti-Tumour Necrosis Factor Treatment

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Introduction: Ankylosing spondylitis (AS) is a chronic inflammatory disease. Thyroid dysfunctions are more frequent in patients with inflammatory diseases. In this study, we aimed to evaluate thyroid functions and thyroid autoantibodies in ankylosing spondylitis patients, to determine the effect of anti-tumor necrosis factor treatment in AS patients and the relationship between thyroid function and autoantibody levels, inflammatory markers and disease activity in ankylosing spondylitis patients.

Materials and Methods: 74 ankylosing spondylitis patients diagnosed according to 1984 Modified New York criteria and Assessment in Spondylarthritis International Society classification criteria were included. 41 of them were receiving anti-tumor necrosis factor treatment and 33 of them were receiving nonsteroid anti-inflammatory drugs. We recorded patients' age, gender, erythrocyte sedimentation rates, C-reactive protein values, blood count, biochemical analysis, thyroid function tests, autoantibody levels, Bath Ankylosing Spondylitis Disease Activity Index.

Results: Mean anti-thyroid peroxidase levels were significant at a high level in ankylosing spondylitis patients receiving anti-tumour necrosis factor compared to patients receiving nonsteroid anti-inflammatory drugs (p= 0.009).Negative correlation was found between thyrotropin-stimulating hormone and C-reactive protein(r=-0,264, p=0,023).A positive correlation was found between free thyroxine and C-reactive protein (r=0,436,p=0,009), anti-thyroid peroxidase positivity and erythrocyte sedimentation rate (r=0,384,p=0,001),anti-thyroglobulin positivity and erythrocyte sedimentation rates and C-reactive protein(r=0,329,r=0,265,p=0,004,p=0,022).

Conclusion: The frequency of thyroid disorder in patients with AS receiving anti-TNF α was lower compared to patients receiving nonsteroid anti-inflammatory drugs. We can consider that anti-TNF α treatment could reduce autoimmune thyroid diseases and had a positive effect on thyroid functions.

Keywords: Thyroid function, ankylosing spondylitis, anti-tumour necrosis factor treatment

Introduction

Ankylosing spondylitis (AS) is a chronic, systemic, autoimmune, inflammatory disease that characteristically affects the sacroiliac joints and spinal column (1). The diagnosis of AS is based on the Modified New York criteria (mNY) and Assessment in International Spondyl-arthritis Society (ASAS) classification criteria (2-3). The systemic lupus erythematosus (SLE) (4), vasculitis (5), interstitial lung disease (6), sarcoidosis (7), multiple sclerosis (8) and auto

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immune liver diseases (9) have been reported as concomitant autoimmune diseases with AS. This has been explained by genome-wide association studies. In these studies, numerous risk loci have been defined for these auto immune disorders (10). Thyroid dysfunctions are also frequent in rheumatic disease patients (11). These diseases are rheumatoid arthritis (RA) (12), SLE (13), Sjogren's syndrome (SS) (14) and AS (15). Lazúrová et al. (12) defined the prevalence of autoimmune thyroid disease (AITD) and anti-thyroid autoantibodies in RA patients. They reviewed the role of genetics in the association of both AITD and RA. Appenzeller et al. (13) reported the association between thyroid dysfunction and SLE. Sun et al. (14) performed a systematic review to demonstrate the risk of thyroid disease in SS patients. They suggested that SS patients should be screened for thyroid disease. Lange et al. (15) investigated thyroid autoimmunity. As a result of their study, the prevalence of anti-thyroid antibody was significantly higher in AS.

In our study, we aimed to evaluate thyroid function tests (TFTs) and autoantibodies, to determine the effect of anti-tumor necrosis factor (TNF) treatment in AS patients and the relationship between thyroid function and autoantibody levels, inflammatory markers and disease activity in AS patients. To the authors' knowledge, this is the first study that evaluated disease activity in AS patients with TFTs and autoantibodies.

Materials and Methods

Ethical Statement

This study was approved by the ethics committee and carried out from July 2016 to December 2016. All participants signed the informed consent form (Approval: 2017-1046).

74 AS diagnosed according to 1984 mNY and ASAS classification criteria were included (2-3). mNY criteria are as following; having at least 1 clinical criterion (inflammatory back pain, limitation of mobility of the lumbar spine, or limitation of chest expansion) plus radiologic criteria (radiographic sacroiliitis; grade 2 bilateral or grade 3-4 unilateral sacroiliitis) (2). According to ASAS criteria AS diagnosis is possible either by using the 'imaging' arm with signs of active sacroiliitis in magnetic resonance imaging (MRI) with at least one other spondylarthritis (SpA)feature or by using the 'clinical' arm, where the presence of human leukocyte antigen-B27 (HLA-B27) is mandatory with an additional two or more SpA features (3). 41 of AS patients were receiving anti-TNF treatment and 33 of them were receiving non-steroid anti-inflammatory drugs (NSAIDs). Braun et al. stated the conditions for treatment with anti-TNF therapy should be the diagnosis of AS (usually by the mNY criteria), active disease (BASDAI>4 and expert opinion) for at least 4 weeks, failure of NSAIDs for a minimum 3-month trial, failure of intra-articular steroids (if indicated) and failure of sulfasalazine (if predominant peripheral arthritis) (16). All participants had data about thyroid hormones and autoantibody levels.

Inclusion criteria were patients who were over 18 years and diagnosed with AS according to Modified NY criteria. Exclusion criteria were (1) pregnancy, lactation; (2) previous thyroid diseases; (3) presence of additional co-morbidity (diabetes mellitus, asthma, chronic obstructive pulmonary or hepatic-renal-vascular cardiac disease, etc.); (4) use of drugs which may cause thyroid diseases. All the patients' age, gender, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) value, TFTs (thyroid

stimulating hormone (TSH), thyrotropin (FT_3), thyroxine (FT_4), auto antibody (anti-thyroid peroxidase (anti-TPO), anti-thyro globulin (anti-TG) and BASDAI scores were recorded.

Ankylosing Spondylitis disease activity was defined according to the BASDAI score. Based on this score, BASDAI<4.0 was defined as low disease activity and BASDAI>4.0 as high disease activity. It includes six items questioning the patient's fatigue, the severity of the neck, back and hip pain, the severity of peripheral joint pain, tenderness on pressure and palpation, and severity of morning stiffness (17). BASDAI scores and laboratory features were recorded in the 3rd month of treatment.

Erythrocyte sedimentation rate' (ESR) normal range was defined as 0-20 mm/h, CRP' as 0-5 mg/L, respectively (18-19). TSH' normal range was defined as 0.35-4.94 uU/ml, FT_3' normal range was as 1.71-3.71 pg/ml, FT_4' normal range was defined as 0.70-1.48 ng/dl, respectively (20). We defined the thyroid status as Euthyroid: TSH, FT_3 and FT_4 levels between the normal ranges, hypothyroid: TSH level over 4.94 uU/ml and FT_4 level lower than 0.70 ng/dl, hyper thyroid: TSH level lower than 0.35 uU/ml and FT_4 level over 1.48 ng/dl (21). Subclinical hyper thyroidism was defined as a TSH level below 0.35 uU/ml with FT_3 and FT_4 levels between the normal ranges. Subclinical hypothyroidism was defined as TSH levels over 4.94 uU/ml with FT_3 and FT_4 levels between the normal ranges (21). Autoimmune thyroid disease was defined as Anti-TPO levels over 5.61 IU/ml and anti-TG levels over 4.11 IU/ml (21).

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) v19. Normally distributed variables were tested with independent T-test, non-normally distributed variables were tested with Mann-Whitney U test. Descriptive was given as mean± standard deviation (SD) and median (25-75 percentiles). $p<0.05$ was considered statistically significant.

Results

The mean age was 42.7±8.6 years in AS patients. There were 31 male, 10 females AS receiving anti-TNF α. The mean age was 41.8± 10.2 years in the NSAIDs group. There were 23 males, 10 females in the NSAIDs. There was no statistically significant difference between groups in terms of demographic features (age and sex), ESR, CRP, complete blood count (CBC), biochemical analysis, TFTs and anti-TG levels ($p>0.05$). Mean anti-TPO levels were significant at a high level in the AS patients receiving anti-TNF α compared to the NSAIDs group ($p=0.009$). Demographic and laboratory features of patients are presented in Table 1.

Table 1. Demographic and laboratory features of the patients with AS

Variables	Anti-TNFα group (n:41)	NSAIDs group (n:33)	p
Age (years)	42.7±8.6	41.8±10.2	
Gender ▪ Male (n) ▪ Female (n)	 31 10	 23 10	
ESR (mm/h)	22 (13.5-30.5)	18 (9-33)	0.267
CRP (mg/L)	7.5 (2.7 -17)	5.3 (1.8 -12.5)	0.504
Thyroid function tests ▪ FT_3 (pg/ml) ▪ FT_4 (ng/dl) ▪ TSH (μU/ml)	 3±0.5 1±0.1 1.1±0.6	 3.1±0.5 1±0.1 1.3±0.7	 0.35 0.485 0.37
Anti-TPO	0.27 (0.18-0.55)	0.11 (0-0.5)	0.009
Anti-TG	1.57 (0.99-2.49)	1.43 (0.92-2.49)	0.556

SD: Standard deviation; ESR: Erythrocyte sedimentation rates; CRP: C-reactive protein; FT_3: Free triiodo thyronine; FT_4: Free thyroxine; TSH: thyroid stimulating hormone; Anti-TPO: Anti-thyroid peroxidase; Anti-TG: Anti thyroglobulin.

A negative correlation was found between TSH and CRP (r=-0,264, p=0,023). A positive correlation was found between FT4 and CRP (r=0,436, p=0,009), anti-TPO positivity and ESR (r=0,384; p=0,001), anti-TG positivity and ESR and CRP (r=0,329; r=0,265; p=0,004; p=0,022) (Table 2).

Table 2. Correlations between Bath AS Disease Activity Index, ESR and CRP levels with values related to thyroid of the patient

Variables	BASDAI	ESR (mm/h)	CRP (mg/L)
FT_3 (pg/ml)			
▪ r	-0,066	-0,209	-0,158
▪ p	0,579	0,073	0,179
FT_4 (ng/dl)			
▪ r	-0,056	0,228	0,436
▪ p	0,636	0.051	0,009
TSH (μU/ml)			
▪ r	0,252	0,133	-0,264
▪ p	0,031	0,260	0,023
Anti-TPO positivity			
▪ r	0,134	0,384	0,153
▪ p	0,256	0,001	0,192
Anti-TG positivity			
▪ r	-0,042	0,329	0,265
▪ p	0,720	0,004	0,022

FT_3: Free triiodo thyronine; FT_4: Free thyroxine; TSH: thyroid stimulating hormone; Anti-TPO: Anti-thyroid peroxidase; Anti-TG: Anti-thyroglobulin; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ESR: erythrocyte sedimentation rates; CRP: C-reactive protein

Discussion

Thyroid disorders which are seen during anti-TNF α treatment can be coincidence or a paradoxical event and at the same time, they may be a marker of immunogenicity (22). The effect of anti-TNF α treatment on thyroid functions is not well known yet.

The study of Lange et al. included 22 AS patients and 22 controls (10). They investigated FT_3, FT_4, total triiodothyronine (TT_3) levels, and anti-thyroid antibodies. As a result of their study, the prevalence of anti-thyroid antibodies was significantly higher in AS patients. Peluso et al. (23) evaluated TFTs and antithyroid anti bodies in 357 spondylarthritis SpA and 318 controls. They announced that thyroid auto immunity was significantly higher in SpA. Acay et al. (24) evaluated TFTs, anti-thyroid anti-bodies in 122 controls, and well-defined 201 patient (including AS). FT_4, TSH, and anti-thyroid antibodies were higher in well-defined patients. Subclinical hypothyroidism was found in 3 patients. The study by Emmungil et al (25) investigated TFTs levels and anti-thyroid antibody positivity in 80 AS patients, 62 Sjögren syndrome (SjS) patients, and 80 healthy controls. The positivity of at least one of thyroid antibodies was significantly more frequent in AS patients (p=0.017). Tarhan et al. (26) studied TFTs and anti-thyroid antibodies. Their study included 44 AS patients receiving anti-TNF α and 64 patients receiving other drugs. As a result of the study anti-TPO level was higher in 23 patients receiving other drugs ($p<0.05$). They announced that autoimmune thyroid disease was lower in patients receiving anti-TNF α.

Tumour necrosis factor α (TNF α) and TNF α receptors have been found in human thyroid tissue (27). This can explain why autoimmune thyroid disorders are seen during anti-TNF α treatment (23). And the frequency of thyroid disorders which are seen during anti-TNF α treatment could be explained by this common pathology.

In our study, we aimed to evaluate TFTs and autoantibodies in AS patients receiving anti-TNF α and NSAIDs. As a result, we found higher anti-TPO levels in AS patients receiving anti-TNF α. Also, we found a negative correlation between TSH and CRP values, while a positive correlation between FT_4 and CRP, anti-TPO positivity and ESR, anti-TG positivity and ESR,

and CRP. The frequency of thyroid disorder in patients with AS receiving anti-TNF α was lower compared to the NSAIDs group. As a result of our study, anti-TNF α treatment could reduce autoimmune thyroid diseases and had a positive effect on thyroid functions. We can consider that when AT disease developed in AS patients receiving anti-TNF α, this treatment could improve thyroid disease. ATPO and ATG

The study has some limitations. The general ability of our findings is limited because of the relatively small sample size. Also, we have not data about anti-TPO and anti-TG values at baseline and at a time after treatment. There is a need for further research with larger samples and long-term follow-up to replicate the findings of this study.

Conclusion

According to our study, we can consider that FT_4, anti-TPO and anti-TG values can be used as inflammatory markers in AS patients. However, we believe that more studies are needed for this research.

Conflict of Interest

The authors have declared no conflict of interest for the present article.

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Trace Element and Lipid Profile in Patients with Type-II Diabetes Mellitus

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Introduction: Impaired trace element metabolism occurs in type II diabetes mellitus (T2DM), suggesting a specific role of trace elements in the pathogenesis and progression of this disease. This study aimed to investigate the relationship between trace element levels and T2DM in patients from Adıyaman province in southeastern Turkey.
Materials and Methods: This study included 49 healthy subjects and 80 patients diagnosed with T2DM. The study population was divided into healthy controls and patients with T2DM and good glycemic control (GGC) and with T2DM and poor glycemic control (PGC). Biochemical parameters and trace element levels were compared in the three groups.
Results: Fasting blood glucose (FBG) and triglyceride (TG) levels were significantly higher in both diabetic groups and were higher in the PGC than in the GGC group ($p<0.05$). Low-density lipoprotein cholesterol (LDL-C) and cholesterol (CHO) levels were higher in the PGC than in the control group ($p < 0.05$). CHO levels were also higher in the PGC than in the GGC group ($p<0.05$). Elevated manganese (Mn) and chromium (Cr) levels were found in both diabetics, and calcium (Ca) levels were significantly higher in the PGC group than in the controls ($p<0.05$).
Conclusions: The hyperglycemic and dyslipidemic profiles were significantly elevated in the PGC group compared to the GGC group, suggesting the importance of regular follow-up and treatment in T2DM. The observed positive correlation between T2DM and the levels of the trace elements Mn, Cr, and Ca requires further confirmation in future studies.

Keywords: Type II, diabetes mellitus, trace element, glycemic control

Introduction

Diabetes mellitus is a metabolic disorder characterized by high blood glucose levels (1, 2). It carries the potential risk of life-threatening health problems that can result in reduced quality of life and increased mortality (3). Type II diabetes mellitus (T2DM) is characterized by hyperglycemia that occurs as a result of insulin resistance, whereby muscle or adipose cells fail to respond adequately to normal levels of insulin (1). High blood glucose levels lead to general vascular damage that affects the heart (4), eyes (5), kidneys (6), and nerves (7) and lead to various adverse complications.

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Unfortunately, the global prevalence of diabetes mellitus is currently increasing and imposing a burden on health systems and national economies. The International Diabetes Federation data in 2017 indicated that 451 million people aged 18–99 years live with diabetes, and this number is estimated to increase to 693 million by 2045 (8). Changes in lifestyle due to urbanization and economic development, which lead to decreased physical activity and increased obesity, now ensure that the prevalence of T2DM will continue to increase dramatically (9).

One complication of T2DM is an impairment of trace metal metabolism (10). Trace elements play an important role in living systems by acting as essential components or cofactors of enzymes that perform regulatory, immunologic, and antioxidant functions in biological systems (10, 11). However, the association between diabetes and impaired trace metal homeostasis remains unclear (2), as trace metal elements could affect the synthesis, secretion, release, and/or mechanism of action of insulin (12, 13). Several ideas have been proposed regarding the relationship between trace elements and T2DM (14-20), but the available evidence is contradictory. This may reflect variations in ethnicity, geographical characteristics, eating habits, and the limitations of the selected study populations. Further studies are therefore required to verify the apparent relationship between diabetes and trace elements in patients with T2DM.

The present study aimed to investigate the relationship between T2DM and trace elements in Adıyaman province, in the southeastern region of Turkey. The selected T2DM patient population was compared with a healthy control group in terms of the biochemical parameters of fasting blood glucose (FBG), cholesterol (CHO), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) and in terms of the levels of the following trace elements: selenium (Se), manganese (Mn), zinc (Zn), copper (Cu), chromium (Cr), sodium (Na), potassium (K), calcium (Ca), and magnesium (Mg).

Materials and Methods

Subjects

This study included a total of 129 individuals consisting of 49 healthy controls without any disorders (including diabetes mellitus) in their medical histories and 80 patients diagnosed with T2DM who were admitted to the Internal Clinic of the Adiyaman University Training and Research Hospital. This study population was divided into three groups: the healthy controls (control group; n=49) and two T2DM groups: patients with good glycemic control (GGC group; n=38) and patients with poor glycemic control (PGC group; n=42). The patients were assigned to the groups with good and poor glycemic control according to their FBG values, as recommended by the American Diabetes Association, with patients with FBG levels ≥7.0 mmol/L identified as the PGC group (21). Pregnant women, individuals under the age of 18, individuals with other chronic diseases (cancer, autoimmune disease, etc.) were not included in the study.

Ethical Statement

The study was approved by the Adiyaman University Ethics Committee (2011/02-1) and written consent was obtained from each subject after the participants were properly informed about the study. All experiments abided by the tenets of the Declaration of Helsinki.

Laboratory Analysis

Venous blood samples were collected into EDTA tubes and centrifuged at 3000 rpm for 10 min. After centrifugation, the blood serum and plasma portion were separated and stored at -20°C until analysis. Biochemical parameters (FBG, CHO, TG, HDL-C, and LDL-C) were measured spectrophotometrically (Advia Centaur 1800, Siemens) from serum samples, while trace elements (Se, Mn, Zn, Cu, Cr, Na, K, Ca, and Mg) were measured by inductively coupled plasma mass spectrometry (ICP-MS; Perkin Elmer, Nexion-350X) from blood plasma samples (22, 23). These results were then evaluated by comparisons between groups.

Statistical analysis

Statistical analyses were performed with SPSS 21 software. Biochemical parameter values and trace element levels of the groups were analyzed by ANOVA and Kruskal Wallis test. After ANOVA analysis, the least significant difference (LSD) and Tamhane's analysis were used for binary comparisons. After Kruskal Wallis's analysis, the Bonferroni correction (Mann-Whitney U test) was used for binary comparisons. A value of $p<0.05$ was accepted as statistically significant for all analyses except the Bonferroni correction.

Results

In our study, a significant difference was observed in all paired comparisons of FBG ($p=0.001$ in all paired comparisons) and TG ($p=0.003$ and $p=0.001$ in GGC-Control and PGC-Control comparisons, respectively). They were observed to be significantly higher in both diabetic groups when compared to the control group. Moreover, FBG ($p=0.001$) and TG ($p=0.013$) levels were found to be significantly higher in PGC group in comparison to GGC (Table 1). CHO levels were observed to be significantly higher in the PGC group when compared to both control ($p=0.001$) and GGC ($p=0.010$) groups. Additionally, the LDL-C level was found to be significantly higher in the PGC group when compared to control ($p=0.002$). No significant difference was observed between the diabetic and control groups in terms of HDL-C level ($p>0.05$). Descriptive data of biochemical analyses were displayed in Table 1.

Study groups were compared in terms of trace elements Se, Mn, Zn, Cu, Cr, Na, K, Ca, and Mg in another phase of the study. Mn and Cr levels were found to be significantly higher in both diabetic groups when compared to the control group ($p=0.001$ in all comparisons in terms of Mn whereas $p=0.001$ and $p=0.002$ in GGC-

Table 1. Descriptive statistic data of biochemical analyses.

Variables		FBG (mmol/L)	CHO (mg/dL)	TG (mg/dL)	HDL-C (mg/dL)	LDL-C (ng/dL)	Age (years)
Good glycemic control (n:38)	Mean±SD	7.2±1.4	195.2±38.1	148.6±65.7	41.6±11.9	125.4±32.3	58.7±10.8
	Med (Min-Max)	6.8 (5.6-10.7)	193.5 (91-287)	136 (36-300)	41 (21-72)	127 (26-196)	59 (34-83)
Poor glycemic control (n:42)	Mean±SD	14.2±5.9	220.7±49.4	191.2±88.5	39.2±7.04	137.05±36.6	55±10.7
	Med (Min-Max)	12.9 (5.9-32)	220.5 (117-318)	174.5 (66-527)	38 (27-57)	135 (63-230)	53 (37-85)
Healthy control (n:49)	Mean±SD	5.2±0.4	180.2±41.8	110.5±51.4	41.6±7.9	113.9±33.7	36.7±14.7
	Med (Min-Max)	5.1 (4.5-5.8)	181 (113-265)	92 (36-277)	41 (29-64)	112 (56-192)	33 (18-78)
P value		*0.001[a]*	*0.001[a]*	*0.001[b]*	*0.374[a]*	*0.007[a]*	*0.001[a]*

SD: Standard deviation, Min: Minimum, Max: Maximum. [a]ANOVA, [b]Kruskal Wallis

Table 2. The comparison between groups in terms of trace elements

Variables	Good glycemic control (n:38)		Poor glycemic control (n:42)		Healthy control (n:49)		P Value
	Mean±SD	Med (Min-Max)	Mean±SD	Med (Min-Max)	Mean±SD	Med (Min-Max)	
Se (ppb)	95.8±19.8	87.3 (64.4-141)	98.8±21.3	98.7 (67.9-173.2)	92.4±19	88.8 (51.6-137.1)	*0.408[b]*
Mn (ppb)	4.9±2.7	4.3 (1.5-13.5)	5.1±2.8	4.4 (1.4-15.5)	2.6±0.9	2.4 (1.3-5.5)	*0.001[a]*
Zn (ppb)	972±140.9	977 (748-1380)	963±189.3	966 (548-1363)	952±216.9	899 (587-1382)	*0.875[a]*
Cu (ppb)	1072±280	1045 (528-1686)	1165±273.1	1195 (632-1681)	1040±290.2	1009 (482-1985)	*0.100[a]*
Cr (ppb)	4.1±2	3.6 (1.3-8.9)	3.5±1.4	3.3 (1-6.7)	2.4±1.2	2.2 (0.1-5.9)	*0.001[a]*
Na (mEq/L)	125.4±17.2	123.7 (93-167.7)	133.5±24.1	131.3 (93.4-199.3)	128.1±23	123.9 (96.8-207)	*0.243[a]*
K (mEq/L)	3.9±0.7	3.8 (2.5-6.2)	4.3±0.9	4.4 (2.8-6.3)	4±0.9	3.8 (2.7-7)	*0.103[a]*
Ca (ppm)	85.3±14.2	83.8 (61.9-117.4)	93.9±21.3	89.9 (65-167.2)	83.2±13.3	81.4 (59.8-125.1)	*0.008[a]*
Mg (ppm)	16.8±3.3	16.7 (11.3-23.7)	17.6±3.6	16.6 (12.1-30.9)	17.7±2.9	17.3 (13-28.3)	*0.421[a]*

SD: Standard deviation, Med: Median, Min: Minimum, Max: Maximum, [a]ANOVA, [b]Kruskal Wallis

Control and PGC-Control comparisons in terms of Cr, respectively). However, no significant differences were observed between GGC and PGC groups *(p>0.05)*. Ca level was seen to be significantly higher in the PGC group compared to the control group *(p=0.021)* when there was not any significance between other pairs *(p>0.05)*. The difference did not reach the level of significance level in terms of Se, Zn, Cu, Na, K, and Mg between study groups (Table 2).

Discussion

T2DM is a chronic disease characterized by insulin resistance, a disorder that is defined as a reduced ability of tissues to respond to insulin as a result of impaired glucose metabolism (17). The resulting hyperglycemic condition due to insulin resistance damages blood vessels and nerve cells and leads to microvascular diseases, such as nephropathy (6), retinopathy (5), and neuropathy (7), as well as cardiovascular disease, which is the major cause of mortality among people with T2DM (4). Therefore, T2DM is a major public health problem that is steadily increasing in response to lifestyle changes due to urbanization and economic development, and that now imposes high economic costs in industrialized countries. T2DM is also associated with impaired trace element metabolism and this impairment may further contribute to insulin resistance and abnormal glucose metabolism (24). Maintenance of trace element homeostasis is therefore essential for the regulation of numerous metabolic events in the human body, including blood glucose levels. Various studies have investigated the relationship between trace elements and diabetes mellitus, but the available data are not consistent and are sometimes even conflicting.

In our study, we compared the biochemical parameters of FBG, CHO, TG, LDL-C, and HDL-C and the levels of the trace elements Se, Mn, Zn, Cu, Cr, Na, K, Ca, and Mg in the GGC and PGC groups and the healthy controls. A significant rise was noted in FBG, CHO, TG, and LDL-C levels between the groups, but no significant differences were noted for HDL-C levels. The FBG levels were significantly higher in both diabetic groups than in the control group, confirming characteristic hyperglycemic condition in T2DM. The FBG was also significantly higher in the PGC group than in the GGC group. Evaluation of the lipid profile between the groups revealed significantly

higher TG levels in both diabetic groups than in the control group. Similar to the FBG results, the TG levels were significantly higher in the PGC group than in the GGC group. Similarly, the CHO level was higher in the PGC group than in either the GGC or the healthy control groups. The LDL-C level was significantly higher in the PGC group than in the control group, whereas the LDL-C level did not differ between the GGC and control subjects, indicating the importance of good glycemic control in T2DM.

Our results are supported by previous studies. For example, Mishra et al. (2017) evaluated fasting plasma glucose (FPG), CHO, TG, LDL-C, and HDL-C levels in both complicated and uncomplicated T2DM groups as well as in healthy control subjects and found significantly higher FPG, CHO, TG, and LDL-C levels in both diabetic groups than in healthy subjects (25). Similarly, Zhang et al. (2017) observed significantly elevated FBG, TG, and CHO levels in a T2DM group than in healthy control subjects, although they did not find any difference in LDL-C levels between their study groups, in contrast to our results (24). Another study also reported significantly higher CHO and LDL-C levels in a T2DM group than in healthy subjects (26). In all these previous studies, the HDL-C level was significantly lower in the T2DM groups than in the control group (24-26). This finding contradicted our results, which indicated a dyslipidemic condition in diabetes, in agreement with other previous studies, and which emphasized the importance of regular glycemic control in the context of maintaining healthy blood lipid levels.

Previous studies have also noted the association between trace element status in T2DM; however, the data show quite notable differences. Some of the previous studies have reported lower Se (27-29), Zn (25, 26, 28-32), and Cu (26, 32) levels in patients with T2DM than in healthy subjects. For example, Nashiry et al. (2019) found lower Se and Zn levels in hair specimens of T2DM subjects who were employed than in samples from non-working subjects. The hair samples also revealed a lower level of Cu in patients with poorly controlled blood glucose. By contrast, the Cu level was lower in patients with good blood glucose control when the analysis was performed using nail specimens (33). Contrary to these studies, Zhang et al. (2017) demonstrated higher Se, Zn, and Cu levels in patients with T2DM than in a control group (24). Similarly, Badran (28) and Oyedeji (29) reported increased Cu levels in subjects with T2DM. Cancarini et al. (2017) found increased Se and Zn levels in serum and tear fluid samples from patients with T2DM (34). Skalnaya et al. (2007) demonstrated elevated Na and K levels, but decreased Mg and Zn levels, in hair samples from patients with T2DM (35). Other studies have reported lower Mg in T2DM than in healthy (24-26, 28-30, 36).

In the present study, we did not find any significant differences between groups in terms of Se, Zn, Cu, Na, K, or Mg levels. Cancarini (34) and Ekmekçioğlu (27) did not report any significant differences in terms of Zn and Cu levels between T2DM and healthy subjects, in agreement with our results. Similarly, Diwan (36) and Hussain (30) did not observe any differences in terms of Zn and Cu levels in a T2DM group and healthy subjects, respectively. Masood et al. (2009) also did not observe any significance between patients with T2DM and healthy subjects in terms of Mg levels (31). Cancarini et al. (2017) did not report any significant differences in Se levels in tear fluid samples from diabetic and control subjects (34).

In our study, we found statistically significant differences in terms of Mn, Cr, and Ca levels between our study groups. The Mn and Cr levels were significantly higher in both diabetic groups than in the healthy subjects. The Ca level was also significantly higher in the PGC group than in the controls, but these levels did not differ from that of the GGC group. Cancarini et al. (2017) observed elevated Mn and Cr levels in the tear fluid samples of patients with T2DM, in agreement with our results. However, serum Cr levels were significantly lower in the patient group but the Mn levels did not differ between the groups (34). Ekin et al. (2003) demonstrated significantly higher Mn levels in patients with T2DM than in healthy subjects (37). In contrast to our results, other previous studies have reported lower Mn (26, 28) and Cr (28, 29, 32) levels in patients with T2DM than in healthy subjects. Skalnaya et al. (2017) also found lower Ca levels from hair samples of patients with T2DM than in healthy subjects (35). Zhang et al. did not report any significant differences in terms of Mn, Cr, or Ca levels between T2DM and control subjects (24). Similarly, Hussain et al. (2009) did not observe any significant differences in Mn levels between T2DM and healthy subjects (30).

Various studies have explored the relationship between trace elements and diabetes mellitus in the past. However, the data obtained are not consistent and are sometimes even conflicting. This may reflect differences in the study populations in terms of ethnicity, geographical characteristics, and eating habits. Therefore, further studies are required to verify the relationship between T2DM and trace elements.

We found dramatically higher FBG levels and dyslipidemia profiles in terms of CHO and TG levels in the PGC group in comparison to the GGC patients. Regular follow-up and treatment improved the chronic hyperglycemic and dyslipidemic conditions, which are the major characteristics of diabetes mellitus. Elevated levels of Mn, which acts as an antioxidant enzyme cofactor in biological systems, may be associated with the increased oxidative stress status associated with T2DM. These elevated levels appear to emerge as a compensatory mechanism that prevents the exacerbation of the disease. Besides, the increase in the Cr level can be interpreted as the body's attempt to augment the activity of the insulin receptor, which cannot take up sufficient insulin into the cells in T2DM. This response, which can also be regarded as a contribution to compensatory mechanisms, prevents disease from increasing in severity by promoting a lowering of the blood sugar levels. The Ca increase was higher in the PGC group than in the controls, and this may be associated with elevated levels of insulin in T2DM. This causes a further release of insulin, thereby further increasing the levels of insulin that already cannot be metabolized. These findings emphasize the importance of glycemic control in combating high insulin levels, a key characteristic of T2DM.

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Conflict of Interest

The authors declare no conflict of interest.

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ORIGINAL ARTICLE OPEN ACCESS

Effect of Endoscopic Correction on the Blood Pressure of Hypertensive Patients with Deviated Nasal Septum Symptoms

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Introduction: The objective of the study is to evaluate the effect of endoscopic correction of the septum on blood pressure in patients with deviated nasal septum symptoms and to assess positive changes that occur between deviated nasal septum and hypertension.
Materials and Methods: The study was conducted and data have collected in the department of ENT, different hospitals at Madinah Munawarah, Saudi Arabia. A total of sixty-eight adults medically examined at the age range between 20 to 45 years, with symptomatic nasal septal deviation, newly detected untreated hypertension (mean BP 140/90 mmHg), undergoing septoplasty operation and submucosal diathermy of the hypertrophied inferior turbinate (when present), were included. Postoperative follow up for ENT examination and BP measurement was done at 1st, 6th month, and the end of the year.
Results: There are 68 patients were taken for this study from various hospitals in the department of ENT, Madinah Munawarah region, Saudi Arabia. Among 68 patients 42 Male and 26 Female patients at the mean age of 35.23±2.15 years with a range of 29 to 44 with respective of male and female. Age distributed in the group as 19% of patients were in 25-30, 43% of patients in 31-35, 22% of patients in 36- 40, and 16% of patients were in 41-45, major fall in the age group of 31-35 years.
Conclusion: We concluded from our study that control of blood pressure in patients with nasal septal deviation can be achieved by surgical correction effectively and safely. Consequently, patients with symptomatic septal deviation should be assured of the prevention of secondary cardiovascular problems due to high blood pressure.
Keywords: Nasal obstruction, deviation, hypertension, blood pressure, nasal septum, ear nose throat

Introduction

The opening of the nose is separated into two passages by the nasal septum. Typically septum is present in between the nostrils. Hence the openings of the nose are proportioned. Deprived drainage from the sinuses can be the effect of the diverged septum of the nose. The blockage in the upper respiratory tract identical to diverged nasal septum and obstruction can lead to respiratory depression. Numerous researchers studied the development of circulatory complications in pulmonary arterial hypertension. Now general population 75 to 80% are predicted to have some types of nasal deformity. Apart from the actual sustenance system of the nose and the main factor of its

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figure, the distance and the lateral walls and the septum of the nasal passage controls the breathing and flow of air in the nose (1, 2).

Deviation in the nasal septum is the most frequent reason for nasal obstruction conferred with a decline in airflow of the nose and chronic irritability in the mucosa (3). Thus anomalous blockage of upper airway could lead to the progression of blood pressure (4). The present classification and definition of hypertension, established on the seventh report of the joint national committee on prevention, detection, evaluation, and treatment of hypertension (JNC 7), stipulates the verge for description (BP) Blood pressure as ≥140/90 mmHg. Finding efficient management of high blood pressure which reduces the pericardial failure, chronic renal disease, cerebrovascular accident, and myocardial infarction (5,6).

There is a well-documented correlation stated first in 1960 of chronic obstruction of the upper airway in children and infants with pulmonary hypertension and right ventricular dysfunction (1). In the research, the outcome of chronic obstruction of upper airways such as adenoid vegetation, hypertrophied tonsils, and nasal polyps on the cardiopulmonary system has existed in studies. However, the outcome of the classic nasal deviation on the cardiovascular system has not been specifically studied. In this study, we aimed to assess the blood pressure of the patients with the deviated nasal septum, who was to be undertaken for endoscopic septoplasty.

Materials and Methods

Ethical Statement &Study Design

An observational study was done from May 2016 to November 2019, at various hospitals in the department of ENT, Madinah Munawarah, Saudi Arabia, the ethical approval of the ethics committees of hospitals were taken following standards of ethics. The informed written consent was taken from sixty-eight adults. The inclusion criteria of the study were of both genders male and females aged 20-45 years, suffering from Symptomatic deviation of nasal septal and recently identified high blood pressure (BP≥140/90 mmHg).

Exclusion criteria were individuals agonized before surgery and after surgical period due to many adenoidal /nasal disorders (sinonasal malignancies, septal hematoma, synechiae, nasopharyngeal mass granulomatous disease, allergic rhinitis, chronic or acute infection of the paranasal sinuses or nose, polyps, hyper trophied middle turbinate, perforated septum, septal hematoma, chonchabullosa), had a prior history of septal or nasal operation, had the craniofacial syndrome, received head and neck radiotherapy, endocrine disorders like acromegaly and hypothyroidism, pregnancy, OSA or its hazards like hypertrophy of adenoid or tonsil enlargement, were recognized hyper tensive or on any antihypertensive medication, pulmonary pathologies, uncontrolled asthma, hazards for high blood pressure for instance smoking, tobacco chewing, high salt intake, alcohol consumption, sedentary lifestyle, familial history of hypertension or cardio vascular disease.

Once the complete patient history was taken, medical examination and nasal endoscopic examination was done for preoperative evaluation. Deformities of nasal septum were classified according to the Dreher scale as following: 0=None i.e. no deviation, 1=Mild deviation i.e. deviation less than half of the total distance to the lateral wall, 2=Moderate deviation i.e. deviation greater than half of the

total distance to the lateral wall but not touching it, 3=Severe deviation i.e. deviation touching the lateral wall.

It was noted when there was compensatory hypertrophy of inferior turbinate. Subjects were relaxed before the measurement of blood pressure. The position for the measurement of blood pressure was half lying/supine, the right arm was used to put the cuff of customary mercury sphygmomanometer and BP was measured three times at the intervals of 10 minutes. The charted three readings were averaged. ''Hypertension'' was demarcated as (SBP) ≥140 mmHg systolic blood pressure and (DBP) ≥90 mmHg Diastolic blood pressure.

A preoperative regular workup was done. All subjects were given prophylactic antihyper tensive orally on the night-time before and morning before the endoscopic septoplasty surgery for the reduction of blood pressure and decrease the chances of bleeding during the operation. After the surgery, the subjects were given analgesics and antibiotics for 1 week and 10 days anti-allergic. Subsequently, the nasal pack removal, two weeks of nasal douching was instructed. The follow up of the subjects was done postoperatively after 1 month, 6 months, and at year-end. During every appointment, ENT and a general medical examination were done and as that of preoperative three readings of blood pressure were recorded.

Results

There are 68 patients were taken for this study from the various hospital in the department of ENT, Madinah Munawarah region, Saudi Arabia. Among 68 patients 42 male and 26 female patients at the mean age of 35.23±2.15 years with a range of 29 to 44 with respective of male and female (Table 1). Age distributed in a group as 19% of patients were in 25-30, 43% of patients in 31-35, 22% of patients in 36-40, and 16% of patients were in 41-45, major fall in the age of 31-35. The nasal septal symptoms are subject to suffered by the patients' duration of 1 to 10 years, the mean of 4.2±1.8 years. The patients have 3 to 6 years with symptoms of 68%, 1 to 2 years with symptoms of 17%, and 15% of 7 to 8 years.

Table-1. Study Characteristics

Patients (n:68)	N	%
Male	42	61.76
Female	26	38.24
Mean Age	35.23±2.15	

According to this study, anterior deviation of septal symptoms was found in 68% of patients, posterior deviation of septal symptoms in 14% of patients, and 18% of patients in both septal symptoms. 26% of patients were with mild septal deviation, while 51% of patients were with moderate septal deviation, and 22% of patients were with severe septal deviation. Among 68 patients 15% of patients were observed and undergone compensatory hypertrophy with respective of 9% male and 6% female.

The mean Systolic BP of pre-septal correction operation was 139.7±1.5 mmHg and Diastolic BP of pre-septal correction operation was 92.08 ±1.3 mmHg. After correction of nasal septum with obstruction, blood pressure was controlled in 80% of the patients and recorded highly significant ($p<0.001$) by t-test in Spss, decrease in Systolic BP, and Diastolic BP. That is 10-15 mmHg decreases in Systolic BP and 5-10 mmHg decreases in Diastolic BP (Table -2). In a further study, 22% of patient's blood pressure remains not controlled followed with surgical correction of septal nasal obstruction, 14% of patient's blood pressure remains unchanged and 7% of

Table-2. Blood Pressure Changes after Septal Correction - *p<0.001 – high significance

Subjects Analysis	Systolic BP				Diastolic BP			
	Min-Max	Mean±SD	Comparison Pre -Post		Min-Max	Mean±SD	Comparison Pre -Post	
			T value	P-value			T value	P-value
Pre-Septal Correction	135-150	139.7±1.5	-	-	90-94	92.08±1.3	-	-
Post-Septal Correction								
30 Days	130-145	132.6±6.5	17.25	0.0001*	85-98	84.2±3.5	18.1	0.0001*
180 Days	125-140	128.3±7.5	15.98	0.001*	82-98	83.1±4.2	16.8	0.0001*
365 Days	120-150	127.8±1.5	14.23	0.000*	75-100	85.1±4.9	14.2	0.001*

patient's blood pressure increased after a year follow-ups. There is a significance found in between the Nasal septum deviation and the variation of blood pressure after surgical correction ($p<0.001$) with moderate septum deviation is highly responsive. Although 12% of patients have no big variation difference between pre and post-surgical correction blood pressure values. Blood pressure and age are also associated and shown insignificance ($p<0.001$) as 58.5% of patient's blood pressure is in high after symptoms correction, most of the fall in at the age group of 36-40 years. No significant difference found between blood pressure and Gender ($p>0.01$; $p=0.25$). There was no complication were seen in this study like septal perforation, deformity, septal hematoma, etc., soon after septum correction or delayed during the follow-ups.

Discussion

The nasal cavity has foothold architecture in the middle called the nasal septum. The blockage in the nose is prevalent due to anatomical anomaly in the septum of the nose (2) and it is the maximum prevalent reason for the blockage of the upper respiratory tract. Diverged septum of the nose along with the blockage has a serious impact on our anatomy aggregately (7). Therefore, there is a disturbance in our normal breathing due to obstruction in the nose, thus limiting airflow towards the lungs (1). The Heart rate and respiratory rate are elevated due to the reduction of ventilation or oxygenation in the lungs. Furthermore, the elevation of rate in the respiration does not permit the adequate interchange of gases in subjects with the diverged septum of the nose.

Substantial changes in intrathoracic pressure, hypercapnia, and hypoxia occur due to the mechanical obstructive changes in the upper airway and diverged nasal septum. This may disturb autonomic cardiac reactions due to stimulation of the sympathetic and parasympathetic system(7). Heart rate elevation occurs due to sympathetic stimulation. In the brainstem, the autonomic neural system controlling region for the respiratory system and heart rate are near to each other, so there is uninterrupted communication among these regions (8). Such instances in the patients of the diverged septum of nose can lead to numerous cardiovascular and pulmonary conditions[7].

The effect in the vessels is thought to be due to carbon dioxide variations in blood and vasomotor center activation. There can be reverse actions of pathways, tougher central effect, which is complete vasoconstriction due to higher levels of carbon dioxide and its effect on vasomotor centers, although there is a direct action of vasodilation. Therefore, Blood pressure can increase because of the inhalation of carbon dioxide(9). In subjects with a serious deviation of septum have persistent contact of mucosa and irritation of mucosa by activation of the afferent path of the trigeminal nerve leading to complicated biological reaction comprising of vasoconstriction, bradycardia, apnea, and respiratory drive inhibition, through the afferent pathway by innervated fibers of somatic receptors, baroreceptors, and chemoreceptors (3).

High blood pressure is a cardiovascular disorder originating from the etiology of interconnectedness and multiple factors. When the subject crosses the verge of well-established blood pressure mark HTN is diagnoses. As per the international guidelines, hypertension is defined as an increase in blood pressure >140 mmHg of systolic and >90 mmHg diastolic pressure (6). The standard guidelines have been used in this study for hypertension. Prevention and treatment of high BP with earlier diagnosis reduces the threat of heart failure, Myocardial infarction, stroke, and chronic kidney disease (5). In this research we included adults below 45 years, studies show that there is a higher risk of essential HTN after this stage. We have included subjects with symptomatic obstruction of the nose as per our study, many researchers have revealed anatomical appearance were related severity of obstruction of nose posteriorly and anteriorly (10). Physical assessment with endoscopy of the nose is a precise diagnostic technique for evaluating the patient with a septal deviation of nose requiring septoplasty surgery. There was a limited value as a diagnostic tool for rhinomanometry due to limited capacity to diagnose only major deviations of the septum in the anterior aspect (2). Consequently, our examination followed careful rectification of nasal septum by septoplasty, lack of a benchmark group is because there is no viable interchange treatment for digressed nasal septum, and morally a placebo treatment couldn't be completed because of acknowledged treatment guidelines for septal deviation. The research exhibited a noteworthy reduction in nasal opposition and a critical increment in most reduced oxygen saturation following resection of veered off nasal septum (11-15). Yuritas et al. in their study found a reduction in autonomic dysfunction that occurred because of nasal septal deviation was found to diminish after careful amendment i.e surgical incisions of the veered off septum (7). Similar outcomes were illustrated in our research, which showed (80%) of subjects profited significantly from endoscopic surgical correction, therefore reduced the mean blood pressure towards normal standards after surgery. The partial airflow limitation is due to the nasal valve which affects the blood pressure (1). Therefore maximum vulnerable is the frontal part of the nose and the critical can be the variance of 1 mm in the lumen (16). Researchers have revealed that the posterior aspect of the nasal cavity can hold an important deviation of the septum, which is deprived of considerable escalation in the resistance of the airway. In distinction with the nasal valve deviation area, there is extra folded resistance

in the nose. The rhinomanometry works and the surveillance of subjects are in agreement with our anterior nasal septal deviation correction of septum surgery (17). These observations coincided with our research as we had 68% 0f anterior septal deviation patients and both types of deviance after nasal septal correction surgically revealed control in blood pressure, while the patients with posterior deviance are 14% with the control in blood pressure after surgery. A study by Stamler *et al*. revealed that with the increase in age blood pressure also increases (18). Likewise, our research revealed 7% of patients found with regular increase in blood pressure after the surgery during follow up period, subjects aged from 36 to 40 years were 58.5% and revealed a relationship in blood pressure and age group.

Conclusion

We conclude from our study that control of blood pressure in patients with nasal septal deviation can be achieved by surgical correction effectively and safely. Consequently, patients with symptomatic septal deviation should be assured of the prevention of secondary cardiovascular problems due to high blood pressure.

Conflict of Interest

The author declares no competing interests.

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ORIGINAL ARTICLE OPEN ACCESS

Influence of Workplace, Location and Experience on Preoperative Routine Viral Screening Tests: A Post-Hoc Observation from an Online Survey

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Introduction: Possible occupational exposure to Human Immunodeficiency type 1 and 2 (HIV-1/2), hepatitis B virus (HBV), and hepatitis C virus (HCV) poses a great apprehension among the perioperative health care providers. Routine screening of these disease statuses is frequent, but it is unknown whether there is an influence of workplace, location, and experience on such routine screening.
Materials and Methods: The present analysis is a post-hoc analysis of a previously conducted online survey from February 2018 to April 2018. One-hundred-ninety responses (86.3% Anesthesiologists, rest surgeons) were analyzed; 88.9% were practicing preoperative viral testing routinely. The influence of workplace, location, and experience on such routine screening was analyzed using Fisher's exact test; two-tailed $p<0.05$ was considered as significant.
Results: Anaesthesiologists working in the autonomous institutes with teaching background were doing less routine practices, yet there were no significant differences among the anesthesiologists and surgeons and no influence of workplace and experience noted.
Conclusion: This mini-survey indicates that routine preoperative viral screening is very frequent and practiced equally by anesthesiologists and surgeons working across different health care setups and having different experiences.
Keywords: Anesthesia, Preoperative Assessment, Routine Testing, Infection, Viral Screening

Introduction

Infections like Human Immunodeficiency type 1 and 2 (HIV-1/2), Hepatitis B virus (HBV), and hepatitis C virus (HCV) pose risks to other patients and health care providers during perioperative care. These infections can be transmitted through body fluids and anesthesiologists, surgeons and other health care providers involved in perioperative care frequently comes in contact with such fluids, and are exposed to the risk of potential infection. Although it is known that precautions prevent exposure, the care of such patients has remained an extra concern to date. Over the last two decades, both the National Institute for Health and Clinical Excellence (NICE) and the American Society of Anesthesiologists (ASA) has come out with evidence-based guidelines for the preoperative laboratory tests have been

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formulated (1, 2). The NICE guideline had also been updated recently in 2016. However, there is no recommendation on mandatory screening or routine testing for viral serology in patients who undergo various surgeries or procedures.

The Centre for Disease Control and Prevention (United States), recommend every case to be considered as a potential positive case (3). In India, this issue is neither covered categorically by any administrative/public health guideline, nor by health insurance policies. These facts lead to a dilemma in the context of pre-operative routine viral screening, and routine preoperative viral screening/testing is very much prevalent in practice (4). The present analysis was conducted to evaluate the relationship between workplace and experience of anesthesiologists and surgeons and ordering routine preoperative viral serological testing.

Materials and Methods

Study Design & Ethical Statement

The present analysis was conducted from the databank of a previously conducted online survey. Approval from the affiliated institute with an exemption for consent was taken for the survey. The present study does not need an Ethical Approvement due to be a survey analysis.The original survey was conducted online from February 2018 to April 2018, was created and conducted using free online survey software and questionnaire tool service from GoogleForms (https://docs.google.com/forms). An email with a link to the online survey was sent to the anesthesiologist, surgeons, and public health professionals, including a few public health administrators affiliated with the different public health organizations across the country (India). The emails were collected from the different institutional websites and societies available in the public domain. Reminder emails were also sent to potential respondents if no reply was received after two weeks of the original email request. Responses were collected anonymously via the survey. For this analysis, we included only the responses of the anesthesiologists and surgeons as they are the concerned health care providers usually responsible for ordering the preoperative tests.

Data concerning the practitioner's hospital, including hospital type, location of the hospital, and experience of the practitioner and their practice of routine serology screening were collected. In the original survey, the responses were directly downloaded from the Google form as an Excel file, and the same excel master chart after deleting the responses of public health professionals/administrators was used. The data were then categorized into different groups based on workplace (i.e. autonomous institute, medical college, private teaching hospital, private non-teaching hospital, and public sector non-teaching hospital), location (i.e. Metro city, Tier-II city, district headquarter and semi-urban) and experience (i.e. more than 10 years, 5 to 10 years and less than five years).

Statistical Analysis

The response of participants in context to routine testing was noted and presented as an absolute number and percentage scale. For analyzing the influence, the comparison was made taking autonomous institute, Metro city, and experience more than ten years as the reference. Fisher's exact test and INSTAT software (GraphPad Prism Software Inc., La Jolla, CA, USA) was used for the purpose. A p less than or equal to 0.05 was significant.

Results

A total of 190 (164 from Anesthesiologists and 26 from the surgeon) responses were eligible for the analysis.One-hundred sixty-nine (88.9%)

of the responders were practicing preoperative viral testing routinely; 5.3% did not want to do but had to do due to institutional protocol, and only 5.8% were not doing the tests. While 10 (6.1%) out of 164 anesthesiologists agreed that they do not want the tests to be done but we're doing the tests as per institute protocol; none of the 26 surgeons expressed so (P 0.362, odds ratio 3.6 with 95% confidence 0.20 – 63.37). Among the anesthesiologists who did not want but were doing due to protocol; 40% were from autonomous institutes, and 60% were from teaching backgrounds (from teaching hospitals, colleges, and institutes). Overall, the difference

Table 1. Workplace, location, and experience-wise distribution of the participants expressed in number and % scale

Workplace / Location / Experience Wise Category [N]	Done n(%)	Not done n(%)	Done due to protocol N(%)
Autonomous Institute [25]	20 (80)	1 (4)	4 (16)
Govt Medical College [75]	70 (93.3)	3 (4)	2 (2.67)
Private Teaching Hospital [28]	26 (92.9)	2 (7.1)	0 (0)
Pvt Non-Teaching Hospital [46]	39 (84.8)	5 (10.9)	2 (4.3)
Public Non-Teaching Hospital [16]	14 (87.5)	0 (0)	2 (12.5)
Metro City [82]	74 (90.3)	6 (7.3)	2 (2.4)
Tier-II City [64]	55 (86)	2 (3.1)	7 (10.9)
District Head-Quarter [21]	17 (80.9)	3 (14.3)	1 (4.8)
Semi Urban [23]	23 (100)	0 (0)	0 (0)
<5 Years [90]	82 (91.1)	4 (4.45)	4 (4.45)
5 - 10 Years [44]	38 (86.4)	1 (2.3)	5 (11.3)
>10 Years [56]	49 (87.5)	6 (10.7)	1 (1.8)

Table 2. Comparison of practices of Anesthesiologists and surgeons using Fisher's exact test

Work Place /location and experience-wise category [N=180]#	Anaesthesiologist [N:154]		Surgeon [N:26]		Two-tailed P
	Done n (%)	Not done n (%)	Done n (%)	Not done n (%)	
Autonomous Institute	14 (93.3)	1 (6.7)	6 (100)	0 (0)	10
Govt Medical College	56 (96.6)	2 (3.4)	14 (93.3)	1 (6.7)	0.503
Private teaching Hospital	23 (92)	2 (8)	3 (100)	0 (0)	10
Private Non-teaching Hospital	38 (90.5)	4 (9.5)	1 (50)	1(50)	0.216
Public non-teaching Hospital	14 (100)	0 (0)	0 (0)	0 (0)	-
Metro city	64 (91.4)	6 (8.6)	10 (100)	0 (0)	10
Tier-II city	43 (97.7)	1 (2.3)	12 (92.3)	1 (7.7)	0.407
District Head-Quarter	15 (88.2)	2 (11.8)	2 (66.7)	1 (33.3)	0.403
Semi Urban	23 (100)	0 (0)	0 (0)	0 (0)	-
< 5 years	70 (94.6)	4 (5.4)	12 (100)	0 (0)	10
5-10 years	33 (100)	0 (0)	5 (83.3)	1 (16.7)	0.153
>10 years	42 (89.4)	5 (10.6)	7 (87.5)	1 (12.5)	10

#does not include the tests done due to protocol

between the surgeon and anesthesiologists in the practice pattern was also not significant, P 0.661. Even the autonomous institutes had a practice of doing the tests in 80% of the time when tests done due to institute protocol were deducted. The test rate was highest in the low experience group (91.1% in the <5 years). The practice pattern of the workplace, location, and experience-wise groups are presented in table 1. Workplace, location, and experience-wise, the practice pattern of anesthesiologists and surgeons were also similar (table 2). The analysis of the total tests done (including the tests done due to protocol) and not done concerning workplace and location, taking autonomous institute and metro city as reference respectively; no statistical difference was noted (table 3). Similar results were also noted in context to experience; total tests done/not done were indifferent in the lower

Table 3. Relation of workplace and location with the practice of viral testing, analyzed using fisher's exact test

Workplace / Location Wise Category [N-Respective Total Number]	Done n (%)	Not done n (%)	Relative risk (95% CI)	Two tailed P
Autonomous Institute [25]	24 (96)	1 (4)	Reference	
Govt Medical College [75]	72 (96)	3 (4)	10 (0.91 – 19)	10
Private Teaching Hospital [28]	26 (92.9)	2 (7.1)	0.96 (0.849 – 1.10)	10
Private Non-Teaching Hospital [46]	41 (89.1)	5 (10.9)	0.92 (0.81 – 15)	0.414
Public Non-Teaching Hospital [16]	16 (100)	0 (0)	14 (0.96 – 1.12)	10
Metro City [82]	76 (92.7)	6 (7.3)	Reference	
Tier II City [64]	62 (96.9)	2 (3.1)	14 (0.96 – 1.12)	0.466
District Head-Quarter [21]	18 (85.7)	3 (14.3)	0.92 (0.76 – 1.11)	0.383
Semi Urban [23]	23 (100)	0 (0)	17 (11 – 1.14)	0.335

$including the tests done due to protocol. n-number, CI- confidence interval

Table 4. Relation of experience with the practice of viral testing analyzed using Fisher's exact test

Experience Wise Category [N]	Done N (%)	Not Done N (%)	Relative Risk (95% CI)	Two-Tailed P
>10 Years [56]	50 (89.3)	6 (10.7)	Reference	Reference
5-10 Years [44]	43 (97.7)	1 (2.3)	19 (0.98 – 1.21)	0.130
<5 Years [90]	86 (95.6)	4 (4.4)	17 (0.96 – 1.18)	0.182

$including the tests done due to protocol. N- total number, n-number, CI- confidence interval.

Table 5. Comparison of testing practices taking autonomous institutes as a reference and analyzed using Fisher's exact

Response	AI [N=25]	GMC [N=75]	Two-tailed P	CH-T [N=28]	Two-tailed P	PH-NT [N=16]	Two-tailed P	Pvt. H-NT [N=46]	Two-tailed p
▪ Yes	20 (80%)	70 (93.3%)	0.115	26 (92.9%)	0.234	14 (87.5%)	0.684	39 (84.8%)	0.742
▪ No	1 (4%)	3 (4%)	10	2 (7.1%)	10	0 (0%)	10	5 (10.9%)	0.414
▪ Done Due To Protocol	4 (16%)	2 (2.7%)	032	0 (0%)	043	2 (12.5%)	10	2 (4.3%)	0.175

AI: autonomous Institute, GMC: Government Medical Colleges, CH-T: Corporate Hospital-Teaching, PH-NT: Public Hospital non teaching, Pvt. H- NT: Private Hospital- nonteaching, N: total number

experienced group as compared to the experience of more than10 years (table 4). However, tests done due to protocol (otherwise was not in favor of doing the tests) were significantly lower in government medical colleges (p=0.03) and corporate teaching hospitals (p=0.04) as compared to autonomous institutes (Table 4).

Discussion

The present analysis showed that the practices of ordering preoperative viral screening tests are very much prevalent in all types of hospitals and across all participants with all levels of experience. Nearly 90% of the participants of any category were practicing it, and this rate is higher than a study conducted by Weber et al (5). They analyzed data of 15,482 adult patients and found that the screening rate was 65%. However, the study also found that the incidence of newly detected infections was low and concluded with a strong argument in favor of omitting routine preoperative screening (5). The argument in favor of doing such tests is also prevalent despite the lower prevalence of infection. A study reporting hepatitis C sero prevalence as 2.11%(95%CI;1.1-5.21) argued that by offering routine screening to patients, surgeons have an opportunity to maintain intraoperative safety (6). However, the argument cannot be accepted as a ground for universal screening as the CDC clearly states that every patient should be taken as a potential positive case and due precautions to be taken (3). The statement of the American College of Surgeons regarding the surgeon and hepatitis and HIV type 1 and 2 also emphasizes on the highest standard of infection control and advises to use the effective sterile barriers, universal precautions, or all bloodborne pathogens (7,8). Thir statement also emphasizes on immunization against HBV for the surgeon for the prevention of infection from patient to surgeons.

Criticisms of the universal screening are not only limited to the cost and universal precaution, but also due to the window period negativity fact (9). Advise to screen for hepatitis and HIV has been given based on the resources available from universal screening in high-resource setups to no screening in poor resource setups. The present study analyses the variation of screening or preoperative viral testing in context to the workplace, location, and experience. Usually, the autonomous institutes and big hospitals of metro cities are high resource setups while the semi-urban place hospitals are resource-poor setups. However, the present study findings suggest that there was no difference in the practice of preoperative viral testing in context to the workplace and location. The present study also found that the experience of the health care provider also did not affect the practice of preoperative viral screening. The striking finding was that nearly 90% of the practitioners were advising the tests.

Among Hepatitis B, Hepatitis C, and HIV-1/2, Hepatitis C bears extra importance as it has the highest incidence of transmission after body-fluid contact. The WHO recommended that HCV serology testing be offered to individuals who are part of a population with high HCV prevalence or who have a history of HCV risk exposure/behavior (10).

Resource consideration is also emphasized by the WHO. The 2014 Guidelines Development Group agreed that the infrastructure for both screening and treatment is necessary for screening to have an impact on key outcomes. Therefore, only screening is not the answer,

especially in a country whose per capita health expenditure is minimal.

The present survey is very much limited with a lower number of responses and a national level survey will be required with a larger sample size for a more comprehensible view, especially for the influence of the workplace.

Conclusion

To conclude, this mini-survey indicates that routine preoperative viral screening is frequent and practiced equally by anesthesiologists and surgeons working across different health care setups and having different experiences.

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Conflict of Interest

The authors declare no competing interests.

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CASE REPORT OPEN ACCESS

Pleurocutaneous Fistulas of Fecopneumothorax: Unusual Complications of Penetrating Thoracic Trauma Due to Zebu Gord

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Introduction: Our case highlights an extremely rare colopleural fistula in the setting of post-traumatic diaphragmatic hernia following penetrating wound thoracic of zebu gord with delayed presentation, suspected clinic-radiologically and confirmed on surgery.

Case presentation: A 60-year old moribund male with three months history of open-chest penetrating due to zebu gord, came to the emergency department with a clinical presentation of sepsis syndrome and a deterioration of the general status. On examination, the patient cachectic presented a fecopurulent liquid drainage from an orifice in the anterolateral region of left hemithorax with necrotizing fasciitis. Chest X-ray showed uncompressing hydro pneumothorax in the left pleural cavity.

Conclusion: The patient we report had the most serious complications of post-traumatic diaphragmatic hernia, fecopneumothorax, pleurocutaneous fistula and necrotizing fasciitis. Emergency laparotomy was carried out. The problem was successfully treated by colon resection anastomosis, pleurostomy and negative pressure therapy.

Keywords: Fistula, diaphragm, fecopneumothorax, pleurocutaneous fistula, intestinal perforation, Sister Leena's sign, thoracostomy, traumatic diaphragmatic hernia

Introduction

Fecopneumothorax due to acute traumatic diaphragmatic rupture is a rare entity but clinical picture is critical. The systematic review of Tien Yew Chern et al. report 12 cases reports in the literature in the past 50 years (1). We performed a literature research, over the past 20 years, by consulting PubMed/MEDLINE using the terms "fecopneumothorax and chest penetrating injury". The search revealed only four reported cases of colopleural fistula associated with diaphragmatic herniation due to chest injury but none following chest penetrating trauma (1-3). Our second search using the terms "fecopneumothorax and pleurocutaneous fistulas" revealed zero results.

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We hereby present a case of a patient referred to Teaching Hospital Ravoahangy Andrianavalona, Antananarivo, Madagascar with conditions to delayed management of chest penetrating trauma to zebu gord which was complicated by diaphragmatic rupture and colonic perforation inside the left hemithorax. The authors discuss the mechanism and the relevance of post-traumatic thoracostomy on diagnosis and surgical management of this complex entity.

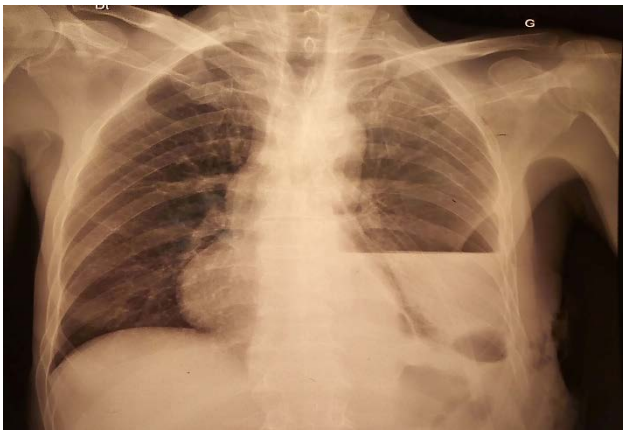

Figure 1. Chest X-ray showing the left-sided potential appearance of hydropneumothorax or pyothorax. Intraoperatively an intrathoracic tension faecothorax recognized and treated.

Case Presentation

A 60-year old male, livestock and arable farmer, with a history of zebu gord, was urgently transferred into the emergency department of our hospital with severe sepsis. A physical examination, the patient's oxygen saturation was 96% and he was spontaneously breathing (23 breaths/min). He had heart rate 120/min, hemodynamic instability status (systolic blood pressure <90 mmHg) without an altered level of consciousness (Glasgow score=15). In chest examination, inflammatory large *open* chest-wall and necrotizing fasciitis on the left hemithorax (7^{th} intercostal space, midaxillary line) was seen. We noticed the outflow of a malodorous fecopurulent liquid

Table 1. Blood results of the patient on emergency admission

Blood Test	Abbreviation	Results		Conclusion
		Patient	*References*	
Haemoglobin	*Hgb*	8,7 g/dl	14 - 18 g/dl	Anaemia
White Blood Cell Count	*WBC*	18×10^3/µL	4,300-10,000 /µL	Leukocytosis and High Neutrophilia
Absolute Neutrophil Count	*ANC*	12,168 (83 %)	1,500-8,000 /µL	
Platelet	*Plt*	536,000/mm^3	150-450,000/mm3	Secondary (Reactive) Thrombocytosis
Erythrocyte Sedimentation	*ESR*	90	<20 mm/h	Infection and Inflammation Due to a Bacteria
C-Reactive Protein	*CRP*	96,5	3 mg/L	
Creatinine	*Creat*	187 µmol/l	74.3-107 µmol/L	Renal Function Failure
Blood Urea Nitrogen	*BUN*	24 mg/dl	14-23 mg/dl	
Estimated Glomerular Filtration Rate	*eGFR*	66,97 ml/min	97-137 mL/min	
Potassium	K^+	5,6 mmol/l	3.5 - 5 mmol/l	Hyperkalemia
Sodium	Na^+	129 mmol/l	135-145 mmol/l	Hyponatremia
Chloride	Cl^-	84 mmol/L	100-108 mmol/l	Hypochloremia

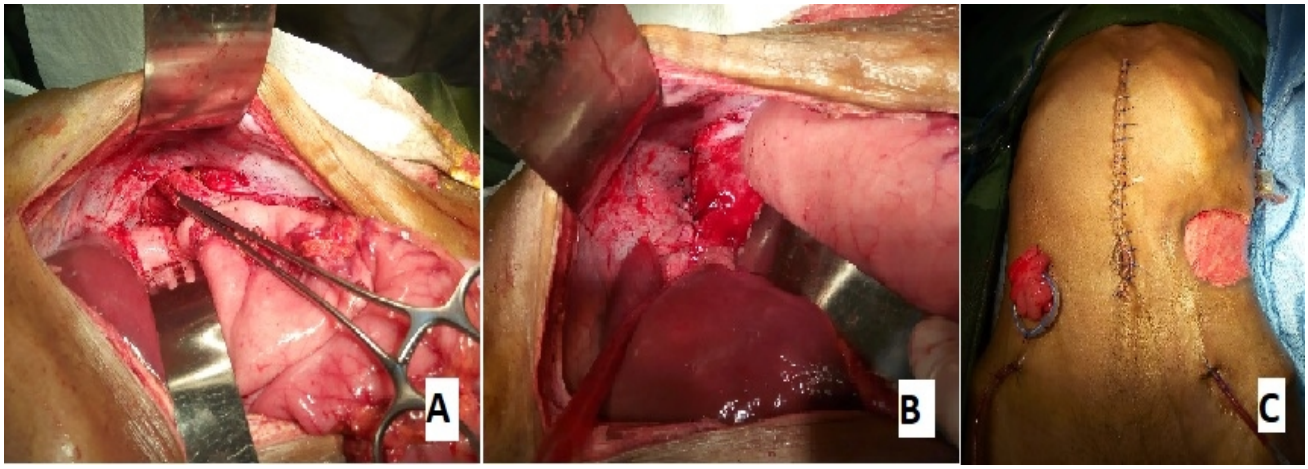

Figure 2. (A) Intraoperative view of the inferior aspect of the diaphragmatic hernia, (B) diaphragmatic rupture after the reintegration of splenic flexure into the peritoneal cavity, (C) Postoperative view of laparotomy and colostomy.

through the orifice and ascaris worm according to interrogation of patient family. Auscultation found a breath sounds decreased in the left hémithorax side. Abdominal and the rest of the examination were unremarkable. Laboratory investigations revealed signs of the severe sepsis (Table-1). Chest X-Ray revealed the potential appearance of hydropneumo thorax or pyothorax with concomitant deviation of the trachea towards the right side. For financial reasons, CT scan was not feasible. The diagnosis of diaphragmatic hernia with colopleural fistula inside the left hemithorax was immediately suspected. Therefore, emergency laparotomy was indicating. Explorative midline laparotomy was performed. Intraoperative findings a 5 cm anterolateral rupture in the left hemidiaphragm with a left colic angle incarcerated and densely adherent into the pleural cavity. After reintegration of colon into the peritoneal cavity through the traumatic rupture of the left hemidiaphragm, there was a perforated and gangrenous colonic segment. The colopleural fistula from the splenic flexure was laboriously mobilized and then resected. The digestive continuity was ensured by termino-terminal anastomosis of the viable colic protected by temporary transverse

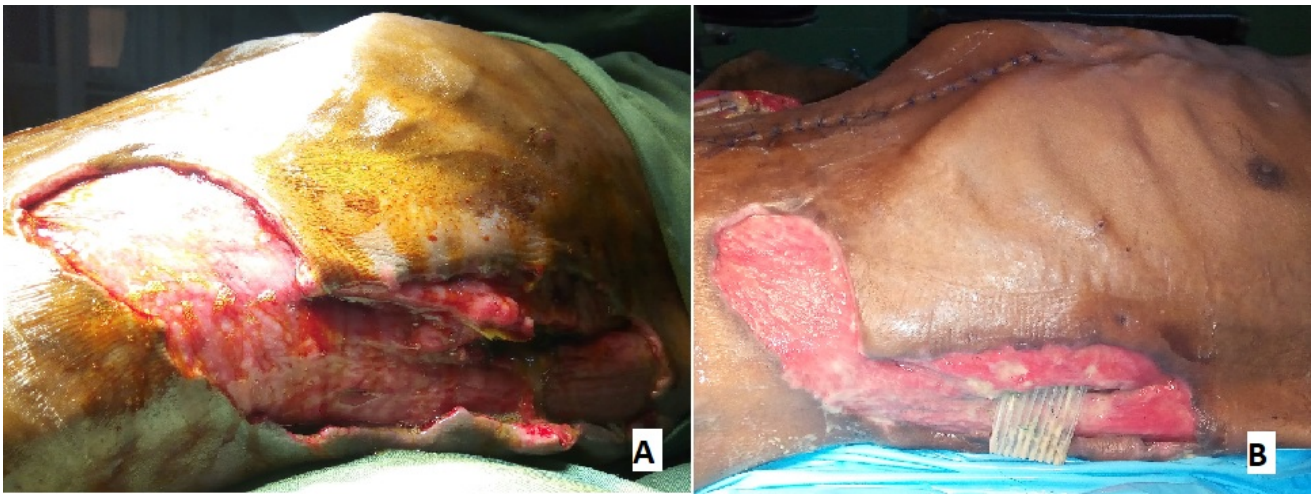

Figure 3. Pleurocutaneous fistulae and necrotizing fasciitis. Sequence of evolution is observed from postoperative day

colostomy requiring a Bogota bag. The defect of hemidiaphragm was repaired with separated non-absorbable sutures. Thoracotomy was not feasible to be carried out because of his unstable haemodynamic status in the lateralised position but the cavity pleura was lavaged transpleurostomy and drained with Delbet drain. For the necrotizing fasciitis, we performed fasciotomy, necrosectomy of devitalized tissue. A homemade closed drainage system (negative pressure wound therapy) was installed with the replacement of the absorbent gauze every 72 hours during 17 days. Three months after discharge from the hospital, the patient is in good clinical with spontaneous closure of thoracostomy and chest radiographic with satisfactory result. Our patient was programmed for colostomy reintegration with an uneventful postoperative course. At follow-up 6 months after surgery, the patient was well and active without restrictive lung syndrome.

Discussion

Fecopneumothorax or fecothorax or faecal empyema is an exceptionally rare but life-threatening condition (4). The first case caused by a colo-pleural fistula was reported by Radin DR et al in 1986 (5). Post-traumatic diaphragmatic hernias complicated with feco pneumothorax are reported with an incidence of 3%, have high mortality rates and require an urgent multidisciplinary approach (6). In literature, penetrating diaphragmatic injury is the most common injury of the diaphragm with a ratio to blunt injury 2:1 (7) and usually results from a stab wound or gunshot wounds of lower thoracic, upper abdomen, or back (8). The specificity of our observation resides in the delayed diagnosis of the diaphragmatic rupture secondary to open penetrating chest wound by zebu gord. This situation is specified in our country as Rabenjamina FR et al confirmed in their work by describing a similar lesion (9). In literature, the authors claim diaphragmatic laceration in penetrating injuries is usually unrecognized during the acute phase because of the lack of symptoms (1, 2, 8, 10). This is due to the small size of diaphragmatic rupture undiagnosed, <1 cm in diameter, in acute episodic and leading herniation of abdominal viscera through the diaphragmatic defect. Secondary colonic perforation is due to ischemia necrosis (8,10) or percutaneous inter costal drainage (11). According to classification of Grimes and al. (12), our case refers to the obstruction phase where hernias have become chronic and complicated. In another hand, except for the delayed diagnosis of penetrating diaphragmatic trauma, some clinical reports have claimed that the sub-diaphragmatic abscess due to malignant tumour, Crohn's colitis, diverticular disease, lung resection may play some role in the formation of colopleural fistula resulting in feco pneumo thorax (13, 14).

If clinical presentation of the incarcerated traumatic diaphragmatic hernia as a "tension fecopneumothorax" (tachypneic, tachycardic, respiratory distress, and possibly hypotensive, the elevation of the jugular venous pressure caused by mediastin) is reported in literature (1, 2, 10). Pleurocutaneous fistulae presented by patient demonstrate the natural progression of this entity resulting in pleurocutaneous fistula never described in the medical literature in our knowledge. The delayed care noted in our case can be attributable by spontaneous pleurostomy that represents vicarious function by decreasing sepsis symptomatology and preventing mediastinal compression for our patient.

The diagnosis of fecopneumothorax remains clinical in our observation but remains very difficult in cases without pleurocutaneous fistula. The published case reports reveal that 18% of blunt and 32% of penetrating injuries are diagnosed in a delayed fashion, generally more than 3 years after the initial trauma and sometimes as many as 40 years later (15). A systematic review of the literature by Rashid et al revealed 17 cases of delayed presentation of diaphragmatic rupture ranging from a period of 24 hours to 50 years (16). A nurse, named Sister Leena, noticed that the amount of purulent drainage was directly related to the amount of the patient's oral intake. She observed that by switching to a parenteral feeding regimen, significantly less volume will be discharged by chest tube drainage. The authors named that observation as the "Sister Leena's sign" and pointed out that this sign may be useful in differentiating colopleural fistula (faecal empyema) from empyema (4, 17).

The diagnosis of diaphragmatic rupture can only be ruled out by direct vision and can be demonstrated operatively in a trauma laparotomy or laparoscopy with a sensitivity of 100% and specificity of 87.5% with the latter (1, 18). Occult injuries do occur in 12-66% due to the difficulty of initial diagnosis and often the absence of symptoms and can be complicated from 2 months up to 50 years (1). If there is no surgical emergency for that in the first step, and in the absence of hemodynamic instability, the diagnosis of diaphragmatic injuries will have to depend on imaging including Chest X-Rays, ultrasound, magnetic resonance imaging (MRI), or computed tomography (CT) (1, 19). In a recent study of diagnosis value of CT scan in diaphragmatic injuries, Yucel M and al. have demonstrated greater sensitivity (82%) and specificity (88%) (15, 20). For the late phase, the simplest and most practical way to establish the diagnosis is by using immediate chest X-ray along with gastrografin enema (2).

Management of this entity is debated in the literature. On the one hand, non-operative treatment advocates who suggest staged treatment, in which improving the patient's health and controlling the sepsis (chest drainage of the pleural empyema, antibiotic treatment, parenteral nutrition) should precede definitive surgical closure of the fistulae for all uncomplicated fistulae if possible (17). On the other hand, Barisiae and al. (19) suggested that surgical treatment is mandatory as soon as the diagnosis is established. A combined thoraco abdominal is the reference approach for several authors for diaphragmatic hernia of delayed diagnosis because the herniated contents tend to be firmly adherent to intrathoracic structures, and this is made worse if bowel strangulation and perforation is present (15). Chatzoulis G et al performed an emergency thoracotomy and laparotomy in their case with a favourable result, which resulted in a very heavy operation (10). In our case, a transabdominal approach enabled closing the defect in the diaphragm resection of the gangrenous and perforated splenic flexure colon with transverse colon colostomy and decortication of the left pleural cavity with lung fully expanded postoperatively.

The pleurocutaneous fistulae avoided recourse to thoracotomy for our patient. The necrotizing chest wall fasciitis was debrided and treated with "homemade" therapy negative pressure. This technique exposes the lesion to a negative pressure by the closed system, favouring microcirculation and improving blood flow and stimulates cellular proliferation of granulation tissue for cicatrisation (21). For our part, we

agree with Kelly and al. (22) and Chatzoulis and al. (10) that the latter diagnosis leads to high morbidity and mortality as seen in several clinical presentations in literature.

Conclusion

Fecopneumothorax is a potential complication following a traumatic diaphragmatic rupture resulting from a zebu gord. The clinical anamnestic elements are useful to guide therapeutic decision and it should be repaired without delay. This observation can be useful for early suspicion of colopleural fistula in the case of fecothorax because perforated colon in these circumstances may present without any abdominal signs. The possibility of a diaphragmatic rupture should always be kept in mind of the physician in the event of penetrating chest trauma to avoid progression to serious delayed complications such as diaphragmatic hernia and fecopneumothorax.

Ethical Statement

The authors declare that the involved patient gave his informed consent for participation in research. The study was done according to the declaration of Helsinki.

Conflict of Interest

The authors declare no competing interests.

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CASE REPORT OPEN ACCESS

A Rare Case: Hyperacute Anterior MI Following Plant-Based Drug Use

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Introduction: Acute myocardial infarction (AMI) is one of the foremost reasons of cardiovascular diseases, which may be fatal in lack of early diagnosis and treatment. Risk factors associated with the disease among the elderly population are fairly straight forward, however among the under-40 age group; they are yet to be unveiled in its completeness. AMI patients under 40 years of age should be questioned especially about cocaine addiction and other drug use in addition to the classic risk factors for coronary artery disease.

Case Presentation: In this case report, we discuss a 35-year-old patient who had Acute anterior myocardial infarction as a result of uncontrolled use of ginseng, lepidium, and epimedium containing herbal medicines due to infertility and who had no other apparent risk factor.

Keywords: Acute anterior myocardial infarction, herbal drug, infertility

Introduction

Acute myocardial infarction (AMI) is one of the foremost reasons of cardiovascular diseases, which may be fatal in lack of early diagnosis and treatment. Risk factors associated with the disease among the elderly population are fairly straight forward, however among the under-40 age group; they are yet to be unveiled in its completeness. AMI patients under 40 years of age should be questioned especially about cocaine addiction and other drug use in addition to the classic risk factors for coronary artery disease. It has been reported that ginseng-containing herbal components boost cardiac activity when used in heart failure and that its chronic use might cause ginseng abuse syndrome with hypertension (1). However, it has also been reported to have hypotensive effects (1, 2). Lepidium extracts, known to be commonly used in the treatment of infertility, are also reported to be cardioprotective (3). Another herbal agent, Epimedium, used especially in Chinese and Korean medicine

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against many diseases, particularly infertility and cardiovascular diseases, is reported to be cardioprotective and antihypertensive (4).

In this case report, we discuss a 35-year-old patient who had AMI as a result of uncontrolled use of ginseng, Lepidium, and epimedium containing herbal medicines due to infertility and who had no other apparent risk factor.

Case Presentation

A 35-year-old male patient was admitted to the ER with the complaint of pressure-like pain which began about half an hour ago and spread to the anterior chest, left arm, and lower jaw. According to the anamnesis of the patient, he had no known disease, had no risk factors for CAD, and did not smoke. Upon questioning regarding drug use, it was learned that he had been using 3 different herbal products containing Lepidium, Ginseng, Epimedium + L-arginine for about a month due to infertility (Figure 1). The patient took these drugs on his initiative under no doctor's control. The patient's ECG was compatible with hyperacute anterior MI (Figure 2). Biochemical tests found out Troponin I as 0.631 ng/ml. Other lab test results were within normal reference values.

Figure 1. Herbal products containing Lepidium, Ginseng, Epimedium+L-arginine

After basal blood values were taken, the patient was taken to the coronary angiography laboratory for primary percutaneous coronary intervention. Coronary angiography showed LAD: total occlusion before DI and CX and RCA to be normal. The LAD lesion was passed with a 0.014-inch floppy wire. When the lesion was passed, it was observed to be with intense thrombus. The patient was administered Ticagrelor 180 mg, acetylsalic acid 300 mg, and heparin 7500 units IV. Intra-coronary abciximab was performed after intense thrombus persisted after balloon (3.5x20mm) predilatation and then stent (4.0x24mm) was implanted at 12 atm (Figure-3).

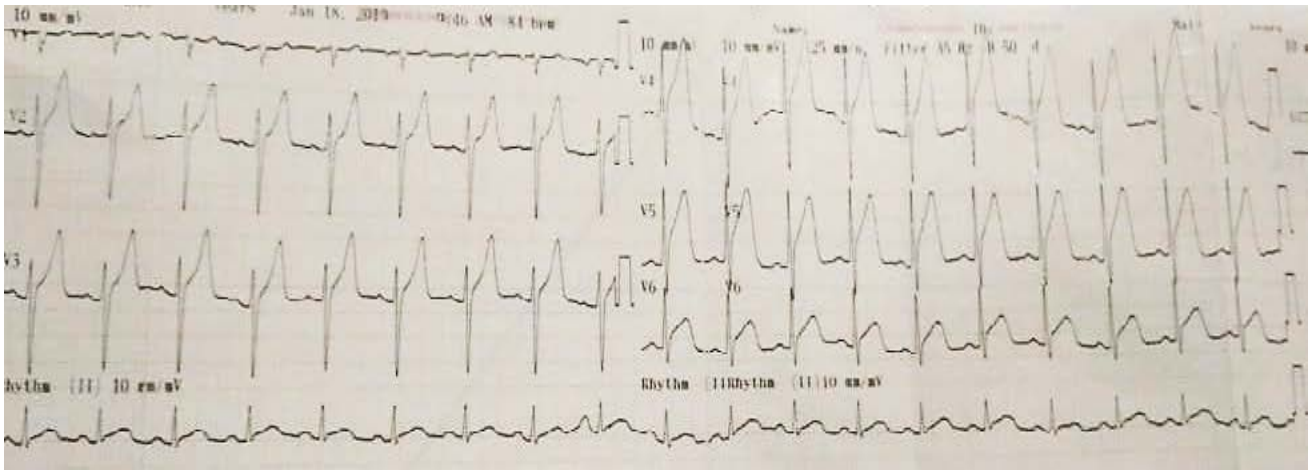

Figure 2. The ECG with Hyperacute AMI

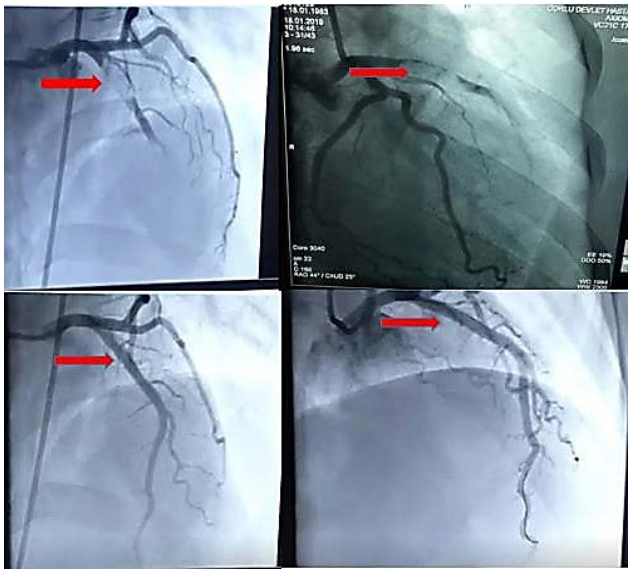

Figure 3. Coronary Angiography

The patient with no complication or complaint in the follow-up was determined to have trans thoracic echocardiography within normal limits and was discharged.

Discussion

AMI is a rare condition in patients under 40 years of age without any risk factors. Drug use should be questioned in this patient group as in our case. It is reported that the herbal agents Lepidium, ginseng, and epimedium, also used in our case, are cardioprotective (1- 4). Besides, it is reported that depending on the dosage, ginseng has such cardiovascular side effects as stent thrombosis and AMI (5, 6). In another study, it was stated that the epidemic reduced reperfusion injury and rehabilitated myocardial functions (7). In light of all this information, we should bear in mind that besides their cardioprotective effect, these herbal agents might have cardiac side effects and we should use them with caution. Especially Panax ginseng is known for its hypotensive effect, however in its chronic use and depending on the dosage, it might trigger what is called "ginseng abuse syndrome" with hypertension, behavior change, and diarrhea. Coronary angiography in our case showed that acute coronary syndrome developed based on dissection in LAD, which led us to consider that labile hypertension might have caused the shear-stress (8-9). Moreover, in our country, the data, whether these drugs are adequately controlled during the certification and production phases, is insufficient and it is not clear whether the indicated doses are correct or not. Studies on the concomitant use of these agents, widely used in infertility, are insufficient. As with this case, we think that the combined use of these herbal agents might be associated with an increased risk of cardiac side effects.

Conclusion

Acute myocardial infarction is rare in patients under 40 years of age without the risk factors. As in our case, drug use should be questioned in patients without any risk factors. In this case, the absence of classical risk factors led us to the conclusion that these herbal agents might have caused the AMI. This case is significant in the sense that it demonstrates the possibly deadly consequences of treatments which are not advised by doctors and are not in line with rational drug use.

Conflict of Interest

The author declares no competing interests.

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CASE REPORT OPEN ACCESS

Arthroscopic Management of Articular Hoffa Fracture: A Case Report

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Introduction: Hoffa fractures are uncommon. These joint fractures require anatomical reduction with stable osteosynthesis allowing early rehabilitation. The arthroscopic reduction with percutaneous osteosynthesis has the advantages of being a minimally invasive technique with minimal morbidity and a good control of the reduction.
Case Presentation: We report here a 35-year-old patient who has a left knee injury after a motorbike accident. The case was treated for Hoffa's fracture by percutaneous fixation arthroscopically assisted with good outcomes.
Keywords: Hoffa fracture, knee articular fractures, arthroscopy

Introduction

Distal femur are uncommon; they represent less than 10% of all fractures of the femur. Unicondylar fractures represent approximately 3% and Hoffa fractures are even unusual with difficult management. These joint fractures require anatomical reduction with stable osteo synthesis allowing early rehabilitation (1, 2).

The arthroscopic reduction with percutaneous osteosynthesis of Hoffa fractures has the advantages of being a minimally invasive technique with minimal morbidity. It also offers a good control of the reduction and allows an appropriate treatment at the same time (6). In recent literature, the published series concerning arthroscopic management of this type of fracture remain limited. We report here the case of a patient treated for Hoffa's fracture by percutaneous osteosynthesis under arthroscopic control.

Case Presentation

A 35-year-old patient has a left knee injury after a motorbike accident. Clinical examination showed a painful and swollen knee (Figure 1). X-rays revealed a displaced Hoffa fracture of

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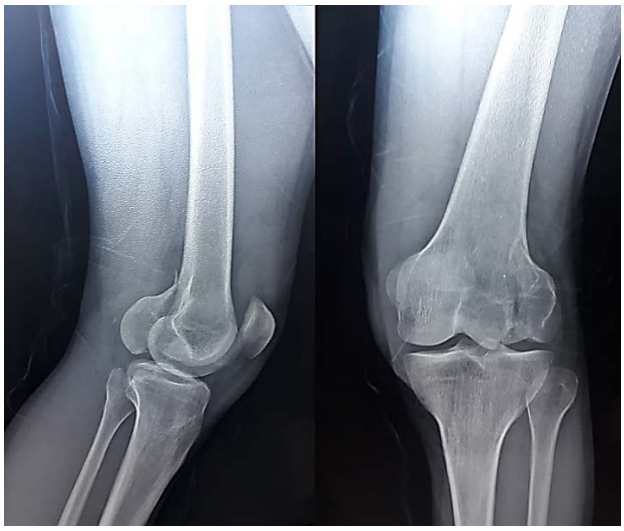

Figure 1. X-rays; Hoffa fracture of lateral condyle

the lateral femoral condyle. The computed tomography confirmed the diagnosis (Figure 2). After patient was planned for an arthroscopic-assisted fixation of his fracture. In the operating room, he was positioned supine with a tourniquet to upper thigh. After evacuation of the hemarthrosis, diagnostic arthroscopy was envisaged (Table 1) (Figure 3).

Figure 2. Computed tomography scan; Hoffa fracture of lateral condyle

The menisci and cruciate ligaments were found to be regular. Joint exploration showed a large Hoffa fracture with osteochondral lesions. The clots were removed by a 3.5 mm shaver and loose fragments were excised (Figure 4).

Table 1. Indications and contraindications

Indications	▪ Recent fractures *Mono-fragment, large volume* ▪ Neglected fractures *Without comminution, large fragment with good bone quality*
Contraindications	▪ Recent fractures *Irreducibility or comminution* ▪ Neglected fractures *Pseudarthrosis requiring grafting*

Fracture reduction was achieved with K-wires used as a joystick. Then, two guide wires were placed in antero-posterior direction (perpendicular to fracture sit). The length and good position of the K-wires were verified under C-arm. Osteosynthesis was carried out by 6.5 mm cannulated screws. Osteochondral lesions were repaired with Herbert screws (Figure 5, 6). The reduction was anatomical and the osteosynthesis was stable (Figure 7). The postoperative suites were simple. Rehabilitation was immediately started with a good recovery of the articular amplitudes. Patient was allowed to bear weight partially at the 6th week. Total bear weight was allowed at the 3rd month. Functional results were very satisfactory.

Discussion

In 1904, Albert Hoffa was the first to describe the typical form for fractures of the femoral condyle in the sagittal plane (3). The therapeutic management of these injuries has undergone a large evolution over the years. Indeed, reduction techniques with internal fixation assisted by arthroscopy appear as new methods providing several advantages (1, 2, 4):

- Surgical aggression is relatively minimal, thus avoiding damage to surrounding tissue, including the risk of iatrogenic damage to the common peroneal nerve.
- The joint architecture can be inspected thoroughly by the arthroscopic control. Consequently, associated lesions (in particular cartilage or ligament damages) can be treated simultaneously.
- The use of a multi-angle screw fixation under fluoroscopic control offers a stable and reliable fixation preventing any risk of rotation or second displacement of the fragment.
- The operating time is shorter, the bleeding is minimal and the risk of infection is so negligible because procedure is performed under continuous irrigation.
- The scar is minimal and conducive to the rapid recovery of the knee joint amplitudes.

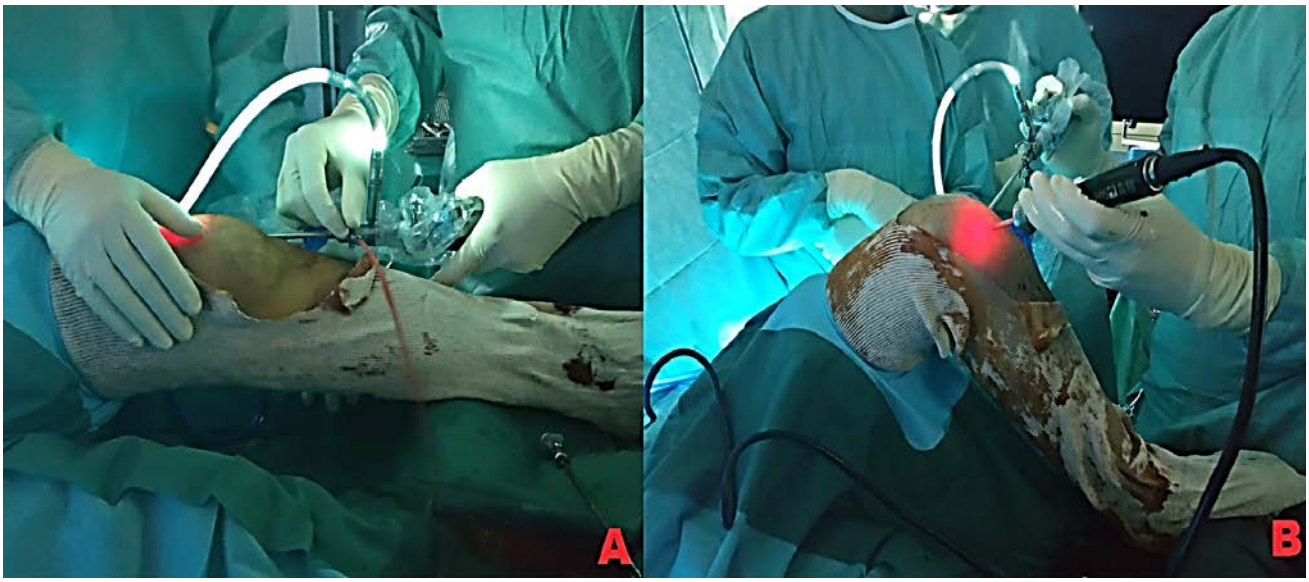

Figure 3. A: Evacuation of the hemarthrosis, B: Diagnostic arthroscopy

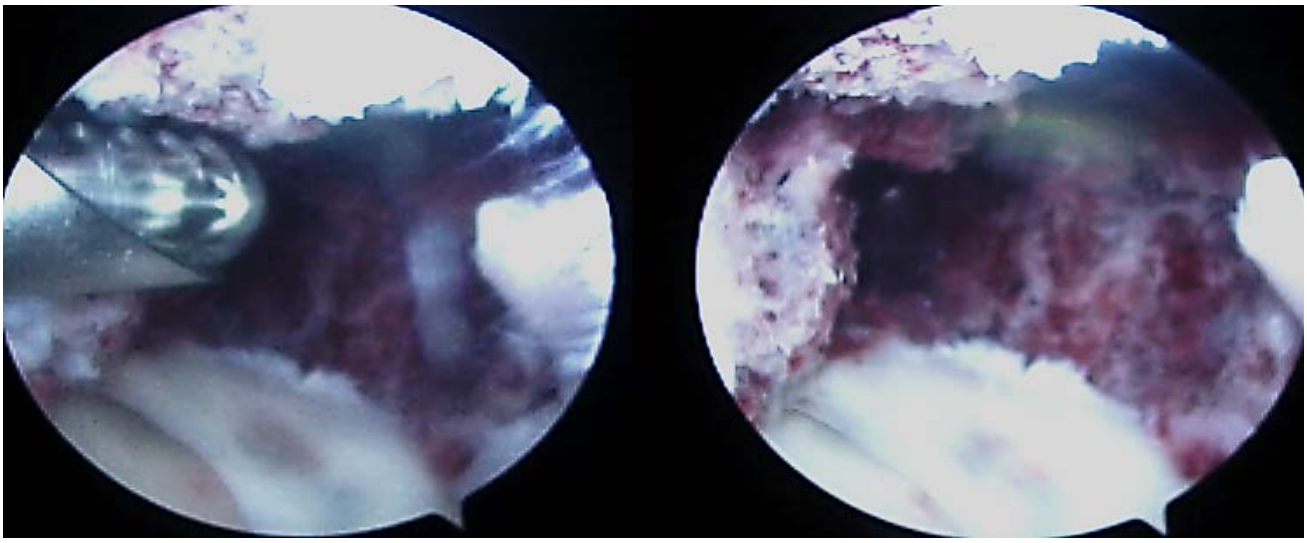

Figure 4. Removing the clots between the fracture surfaces by a 3.5 mm shaver

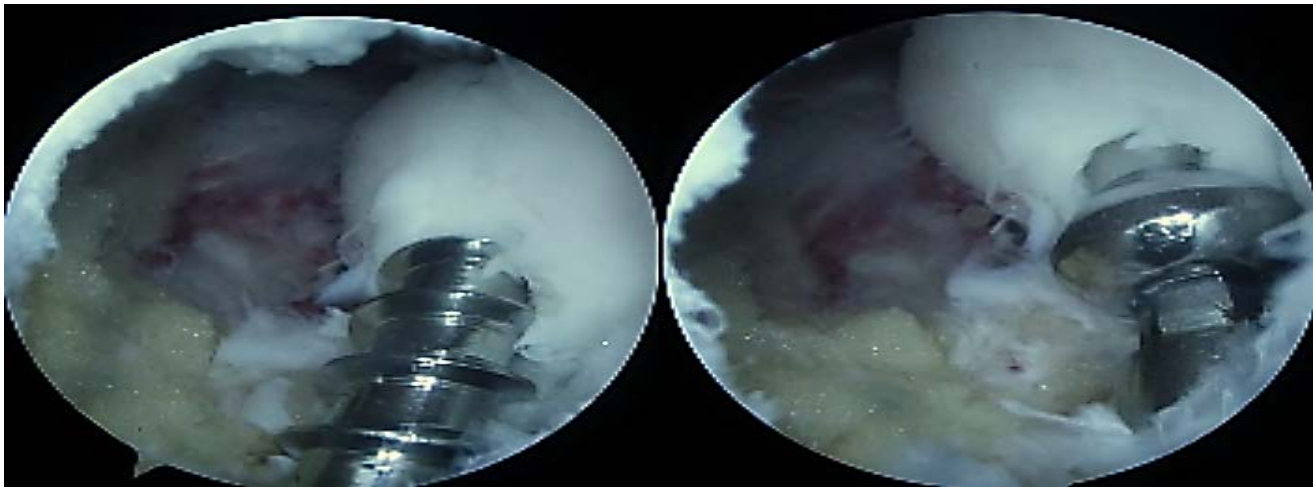

Figure 5. Osteosynthesis of the fracture by 6.5 mm cannulated screws

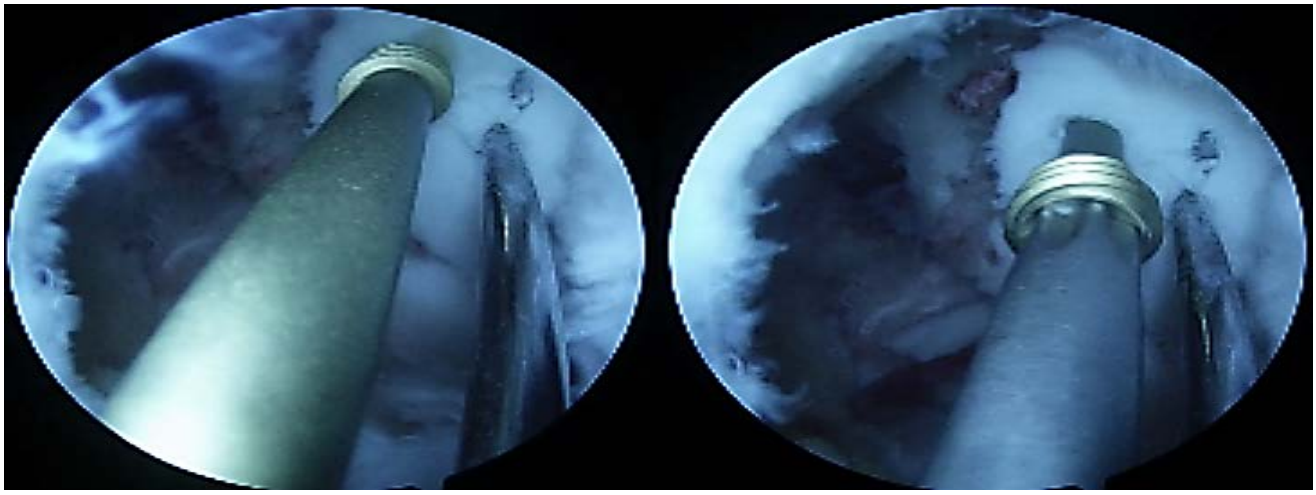

Figure 6. Reparation of osteochondral lesions with Herbert screws

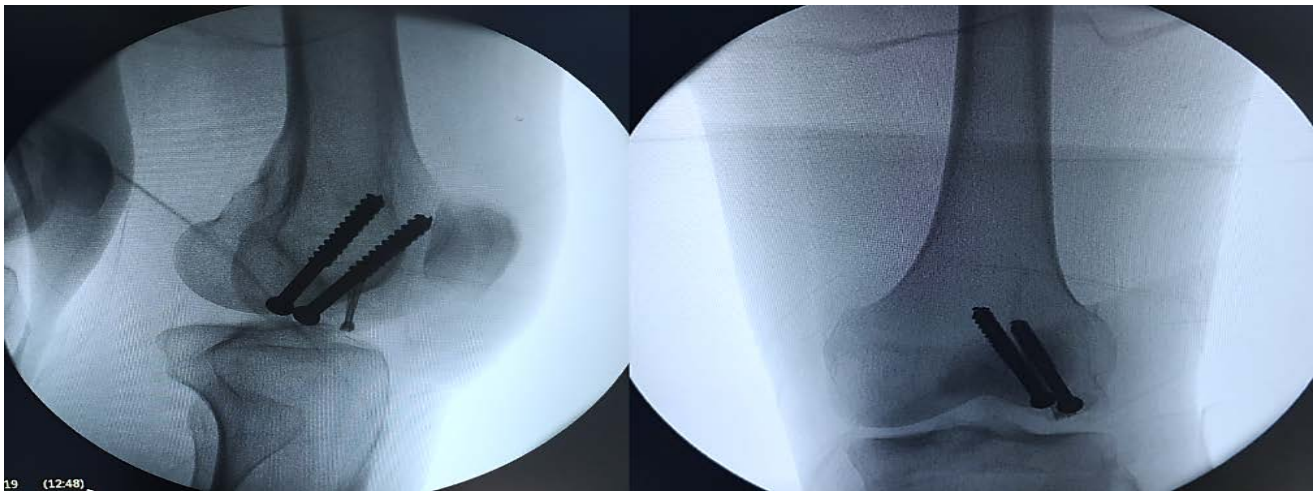

Figure 7. Final fluoroscopic control

The procedure is performed under spinal anesthesia; patient is installed in supine position with a tourniquet to upper thigh. Conventional arthroscopic approaches are used.

After evacuating the hemarthrosis (Figure 1; A), a first diagnostic-look is made (Figure 1; B). The cartilage, menisci and ligaments lesions are checked. The clots between fracture surfaces are excised by a shaver. Generally, the condylar fragment moves retro-femur due to its posterior capsular attachments. A 120° knee flexion relaxes the posterior capsule and the gastrocnemius muscles, thereby reducing the fracture using a simple curved Halsted forceps.

A Kirschner wire can be used as a joystick to assist reduction maneuvers. Also, tibial plateau contributes to the repositioning of the fragment by pushing it back during hyperflexion. The quality of reduction is carefully controlled by magnification offered by the arthroscope camera. The condyle is then temporarily stabilized with two guide pins inserted obliquely and oriented medially and anteriorly from the most posterolateral point of the fragment, just above the lateral meniscus. The final fixation is achieved by 6.5mm cannulated screws following the path of the guide wires. A minimum of 2 screws is required to ensure the rotational stability of the fragment. The screw heads must be inserted through the articular cartilage. The small comminuted fragments are generally removed while the larger are anatomically fixed using Herbert screws under arthroscopic control. The reduction and alignment of the screws are confirmed by intraoperative fluoroscopy. A stability test is then performed by bending the knee up to 140°.

In the postoperative, walking without bear weight is allowed on the second day of surgery. Full weight bearing is allowed from the 12th week. The functional results are globally satisfactory and remarkable (1, 2, 4 - 6) which makes this surgical technique as an excellent therapeutic option in selected patients.

Few reports of arthroscopic assisted fixation of Hoffa fractures are available. Wallenbock and Ledinski reported on a series of 24 intraarticular knee fractures surgically treated two Hoffa injuries (7). They confess the demanding and challenging nature of the arthroscopic fixation. However, they report good early results. McCarthy reported a sagittal plane lateral femoral condyle fracture (8). They were not able to achieve adequate reduction but acclaimed the decreased blood loss, soft tissue dissection, operative time, and the accelerated recovery time. Arthroscopy has been described as a useful tool in the treatment of neglected Hoffa fractures without bone loss (9-11). It also wells as a great treatment for intra-articular and ligamentous injuries which could be not recognized by clinical exam, CT-scan or MRI.

Conclusion

Arthroscopic-assisted osteosynthesis of Hoffa fractures is a technically demanding surgical method, most often applicable for fresh and simple fractures. However, despite its long learning curve, its limited and poorly coded indications, this treatment promises multiple advantages. It reduces the rate of complications encountered with open surgery and thus offering broad prospects for the management of these joint fractures.

Conflict of Interest

The authors declare no competing interest. The patient gives his informed consent to publish this case.

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SHORT COMMUNICATION OPEN ACCESS

Mental Morbidity Arising From Social Isolation During Covid-19 Outbreak

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Introduction

Health, as stated by the World Health Organization (WHO), "is the state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (1) The global outbreak of infectious diseases such as Coronavirus disease 2019 (COVID-19) are usually accompanied with symptoms of mental illness and psychological trauma (2). The circumstance of COVID-19 has presented a series of mental health issues to different groups of individuals, patients, and their families, health workers, students, and indeed almost all sectors of human endeavors (2). Mental health can be summarized as a condition of well-being in which an individual realizes their abilities and can cope with stress as well as being productive (3). Poor mental health can be due to worry, stressful work conditions, social exclusion or isolation, and unhealthy lifestyle (3). This is more than a mere absence of mental disorders but an integral part of health that can be influenced by multiple social, psychological, and biological factors (3). Since the emergence of COVID-19 isolation and quarantine have been greatly employed as a means of curbing its spread (4). The severity of isolation and quarantine varies from clime to clime. However, in the medical context, Isolation is the practice of isolating an individual known to be contagious from non-infected individuals, usually within a health facility, for the duration of the illness while quarantine confines people who have been exposed to a contagious disease for the disease's presumed incubation period (4). These have the potential for instigating mental health challenges like depression, insomnia, fear of the unknown stress, and worry (5).

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Coronavirus disease 2019 was first reported to have been transmitted from animal to human in Wuhan city of China, which was the first world epicenter of this disease in December 2019 (6). Subsequent mode of transmission between human-to-human occurred through inhalation or contact with droplets from infected persons or contacts with infected surfaces. This virus has an incubation period of 2-14 days and its symptoms are usually fever, cough, sore throat, short breath, fatigue, among others (6). The rate of transmission and infection of COVID-19 is alarming across the world, and as of 2 June 2020, there are 6,325,303 cases of infected people including medical workers, 2,727,679 recoveries, and 377,460 deaths globally (7). Early detection, diagnosis, treatment, and isolation are efficient prevention and control guidelines to mitigate the spread of COVID-19 among humans (4). Diagnosed coronavirus is usually isolated to curb transmission. This, however, can make them be subjected to a form of social and or emotional isolation.

Social isolation refers to the lack of contact and interaction or insufficient quality and quantity of social relationships (8). This often leads to loneliness, an unpleasant state of mind where there is a deviation from the desired and achieved manners of social relation (8, 9). Healthcare workers just like isolated patients are operating under the same environment during this pandemic and are therefore vulnerable to mental health-related issues. Social isolation has been recognized with cognitive decline and Alzheimer's disease (10). Loneliness in the COVID-19 context may mean feeling lonely rather than being alone due to separation from normal social networks during isolation and may become a prodrome of dementia which is a deviation from mental health (10).

In retrospect, outbreaks have a great negative psychological impact on people at different levels with the muddling of new psychiatric symptoms in individuals without mental illness (2). Also, the proliferation of the state of those with mental illness and notable psychiatric morbidities ranging from dementia, depression, panic attacks, worry, somatic symptoms, and posttraumatic stress disorder symptoms like psychosis have been discovered (9). Findings have revealed that long periods of isolation can lead to increases in psychological disturbances (9). During the Severe Acute Respiratory Syndrome (SARS-CoV) outbreak in Singapore 2003, it was revealed that some health care workers exhibited symptoms of psychiatric disorder as a result of stress experienced during service delivery. In the same year, a higher number of healthcare workers in the emergency department and the psychiatric ward also manifested post-traumatic stress disorder in Taiwan (5).

Furthermore, part of the aftermath of the 2015 Middle East Respiratory Syndrome outbreak in Korea revealed post-traumatic stress disorder (PTSD) showed by medical staff as a result of work-related stress. Some infected patients with kidney diseases also revealed a reduction in the values of their hematocrit which may result in anemia. The drop seen in the volume of some ions like calcium and phosphorus may lead to osteoporosis. All these are indicators of psychophysical stress and mental distress (5).

Stress and mental morbidity may be as a result of uncertainty, wrong information, and social isolation during this outbreak. The economic impact of COVID-19 such as job loss, low and no income has caused fear and anxiety which harms mental health. Furthermore, it has been discovered that health anxiety starts from the

wrong analysis of sensations and changes felt from the body which becomes a plethora during disease outbreak when there is misinformation is associated with the mental health problem (2). Psychosocial supports are very important during this COVID-19 outbreak to alleviate mental stress. People affected by the outbreak should be given emotional support, compassion, and a sense of belonging to reduce the disease stigma which has a positive impact on mental health and recovery.

Moreover, public sensitization with the right information about the disease should be disseminated to the public, most especially how it can be contracted. Preventive and safety guidelines should be properly communicated to help alleviate the fears of the unknown on the patient, health workers, families, and friends as well as the general public (1). Media channels should be guided to guide against misinformation and rumors, but to uphold messages of hope with emphasis on rates of recovery which will have a high impact on the recovery of other patients. Prompt medical attention should be given to older adults and those with cognitive decline because they are vulnerable to stress, anger, and worries during this outbreak. Patients with history of mental health challenges should also be given urgent attention as at when needed during this period (1).

Conclusively, these measures are expedient because stress associated with COVID-19 may have a long-term effect on the mental health of the patient, and the society at large. These effects may take months before it becomes fully evident; therefore, its management demand joint energy and synergy of the health care system, government, and other stakeholders. Also, unrestricted freedom to quality health and psychosocial support services is highly encouraged and should be readily available to them.

Conflict of Interest

The authors declare no competing interests.

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LETTER TO THE EDITOR OPEN ACCESS

Protecting Doctors Aged Greater than 50 Years from COVID-19

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Dear Editor,

Health, in one recent study (1), Glynn raised the concern about the need of protecting worker aged 60-69 year from COVID-19. In addition to general population, we think this issue is important within healthcare system. However, we wonder whether this estimation can be applied in the healthcare system. To answer this question, we used the same model (2, 3), to estimate the distribution of death according to the doctors' age group. First, we found that 40% and 30% of deaths are in the 70+ and 60-69 year group. Second, after excluding the doctors aged more than 70 years, it estimated that 48% of deaths developed in the 60-69-year age group (Table-1). Both of these findings were consistent with Glynn's findings and suggest that doctors aged over 60 years should be protected. Moreover, we also noted that 31.4% of deaths was estimated to occur in the 50-59-year groups in the group aged less than 70 years. This ratio was higher in the analysis of general population by Glynn, in which 25% of death developed in the group aged 50-59 years. Overall, it suggested that doctors aged greater than 50 years should need protection within the hospital in this COVID-19 pandemic. To avoid overload of healthcare system, which was associated the poor outcome of critical COVID-19 patients and prevent the death of aged physicians, appropriate allocation of

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Table 1. Estimated deaths by age-group if doctors in UK are infected with SSARS-CoV-2

Age	No. of Doctors	Portion of Doctors (%)	Infection Fatality Rate (%)	No. of Death of Patients Infected	Portion of Death (%) If Over 70s Successfully Cocooned
20-29	37967	12.6	0.031	12	1.1
30-39	90256	30	0.084	76	7.1
40-49	80399	26.7	0.161	129	12.1
50-59	56233	18.7	0.595	335	31.4
60-69	26551	8.8	1.93	512	48
70+	9652	3.2	>4.28	>676	-

physicians' works according the specificity and age (<50 vs ≥50 years) should be conducted to enhance effectiveness of healthcare resource.

Conflict of Interest

The authors declare no competing interests.

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