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**RESEARCH ARTICLE**

# Prevalence of catheter related central vein stenosis in hemodialysis patients (two centers study)

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## *Abstract*

**BACKGROUND**: Central vein stenosis (CVS) is a common complication of central venous catheter (CVC) insertion. Placement of a central vein catheter for dialysis access substantially increases the risk of CVS. **OBJECTIVE:** to determine the prevalence of catheter related CVS in hemodialysis (HD) patients and its relation to duration of chronic kidney disease(CKD), catheter site, dwell time insertion, number of catheters, time from catheter removal, catheter infection and Acetyl salicylic acid (ASA) use. **METHODS**: This included 200 haemodialysis patients from those attending to the dialysis units in Zagazig university hospitals & in health insurance hospital (Elmabarra) with previous history of at least one central vein catheter insertion for HD in the period between May 2013 to August 2014.The patients were divided into 2 groups according to doppler ultrasound results: **Group A (with venous stenosis)** : It included 64 patients (36 males and 28 females) with age range (17 to 74 years) with X±SD of 40.7±13.9 years and **Group B (without venous stenosis)**: It included 136 patients (74 males and 62 females) with age range (18 to 75 years) with X±SD of 42.2±14.2 years. Also both groups were classified as regard to duration of CKD, catheter site, dwell time insertion, number of catheters, time from catheter removal, catheter infection and ASA use. All patients were enrolled after written informed consent. **RESULTS**: We found a prevalence of 32% of stenosis following catheterization of central vein in our study patients. We could not find any difference between the patients with and without stenosis regarding age, sex and duration of CKD, however, there was a significant difference in prevalence of stenosis regarding the type of central vein of 20% in subclavian vein and 12% in internal jugular vein, ($p<0.05$). We found a statistically significant increase in CVS regarding dwell time of catheter insertion, number of catheters insertion in one site, frequency of catheter infection and time from catheter removal when comparing both groups of patients. Regarding the role of ASA use in minimizing the occurrence of CVS, we found a statistically significant increase of CVS with less use of ASA when comparing both groups. **CONCLUSIONS**: CVS is not a rare problem in patients on hemodialysis in the two units of the study; infection, repeated cannulation, subclavian vein more than internal jagular vein type and prolonged dwell time of catheter insertion are risk factors for development of CVS and administration of ASA in low dose seems to lessen the occurrence of CVS.

## Introduction

Patients undergoing hemodialysis need chronic vascular access to provide repeated access to the circulation with minimal complications. Complications associated with vascular access include stenosis and thrombosis, infection, digital ischemia, heart failure, pseudoaneurysm and aneurysm. Central venous cannulation can lead to the development of central venous stenosis. In patients on dialysis, this is primarily related to the placement of an ipsilateral central venous catheter but can also occur without a previous history of catheter placement **(1,2).** It is expected that central venous cannulation leads to intimal injury associated with focal endothelial denudation, increased smooth muscle cells and vein wall thickening. Central venous access devices are necessary part of designed treatment plan for many medical conditions such as end-stage renal disease (ESRD), malignancy, intravenous nutritional support and conditions requiring parental therapy **(4).** These devices could be complicated in many ways; the two major complications are infection and thrombosis**.** Occurrence of the latter in temporary central venous catheters is especially troublesome because it limits using vessels of the arms on the side of catheterization for creating fistulas (AVF) or grafts (AVG) in future so it can present major health problems and many international guidelines are instituted for central vein insertion e.g. the American Society of Anesthesiologists **(5).**

These catheters are non-cuffed non- tunneled catheters used in emergency cases of dialysis, in the presence of malfunction of the permanent vascular access or when the patient needs hemodialysis, but created arteriovenous fistulas (AVF) or grafts (AVG) is not mature enough to be used **(6**). Only a small proportion of patients with thrombosis become symptomatic after catheterization. They present with extremity massive pain and edema. However, many patients remain asymptomatic till creation of AVF or AVG, which result in high blood flow in the vein having stenosis. This is the time when many patients, previously asymptomatic, reveal complications **(7, 8**). In addition to symptoms, stenosis can result in inadequacy and failure of AVF and AVG as accesses for hemodialysis on the side of catheterizations.

## PATIENTS AND METHODS:

This work had been carried out in nephrology unit of Internal Medicine department, Faculty of Medicine, Zagazig university hospitals and in nephrology unit of Elmabarra health insurance hospital in Zagazig.

**Study design:**

This cross sectional study included 200 hemodialysis patients from those attending to the dialysis units in Zagazig university hospitals & in health insurance hospital (Elmabarra) with previous history of at least one central vein catheter insertion for HD in the period between May 2013 to August 2014.

The patients were divided into 2 groups according to Doppler ultrasound results:

- **Group A (with central venous stenosis)** : It included 64 patients (36 males and 28 females) with age ranged from 17 years to 74 years with mean values ± SD of 40.7±13.9 years.
- **Group B (without central venous stenosis)**: It included 136 patients (74 males and 62 females) with age ranged from 18 years to 75 years with mean values ± SD of 42.2±14.2 years.

Also both groups were classified as regard to duration of CKD, catheter site, dwell time insertion, number of catheters, and time from catheter removal, catheter infection and Acetyl salicylic acid use.

All patients were enrolled after written informed consent.

**Exclusion critieria :**

Any patient with history of venous disease related to any other cause or in any other site than those used for HD catheters was excluded .

**Methods:**

All patients of the study were subjected to the followings:-

**A) Full medical history** taking and thorough clinical examination: According to checking patient's records.

**B) Routine investigations:**

They were all done according to the methods applied in the clinical pathology laboratories of Zagazig university hospitals and included:

1- Complete Urine analysis.
2- Complete blood picture.
3- Random plasma glucose level.
4- Liver function tests.
5- Serum creatinine, blood urea nitrogen (BUN) by colorimetric method.

**C) Specific investigations:**

- Color Doppler sonography for related central veins in patients on hemodialysis.
- Duplex ultrasound combines Doppler flow information and conventional imaging information, sometimes called B-mode, to allow physicians to see the structure of blood vessels. Duplex ultrasound shows how blood is flowing through vessels and measures the speed of the blood flow. It can also be useful to estimate the diameter of a blood vessel as well as the amount of obstruction, if any, in the blood vessel.

Conventional ultrasound uses painless sound waves higher than the human ear can detect that bounce off of blood vessels. A computer converts the sound waves into two-dimensional, black and white moving pictures called B-mode images. Doppler ultrasound measures how sound waves reflect off of moving objects. A wand bounces short bursts of sound waves off of red blood cells and sends the information to a computer. Doppler ultrasound produces two-dimensional color images that show if blood flow is affected by problems in the blood vessels, such as cholesterol deposits.

When performing duplex ultrasound, physician uses the two forms of ultrasound together. The conventional ultrasound shows the structure of blood vessels and the Doppler ultrasound shows the movement of red blood cells through the vessels. Duplex ultrasound produces images that can be color coded to show physicians where blood flow is severely blocked as well as the speed and direction of blood flow.

According to the Doppler results the patients are classified into two major groups; group A with venous stenosis (64 patients), and group B without venous stenosis (136 patients).

**Statistical analysis:**

Data were analyzed with SPSS version 15.0 (statistical package for the Social Science, Chicago, IL). Quantitative data were expressed as mean ± standard deviation (SD) or standard error (SE). SE=SD/square root of patients number which was used in case of big SD, data were analyzed by independent sample, paired t test and one way analysis of variance (ANOVA). While qualitative data were expressed as number and percentage and were analyzed by Chi square (X2) test. 95% confidence interval (CI) was performed. Multiple regression analysis to find the predictors that were significant to the model. P-value was considered significant if <0.05 and highly significant if <0.001.

## RESULTS:

The clinical and demographic data of studied groups [**Group A (with central venous stenosis)** & **GroupB(without central venous stenosis)** ] are presented in **Table (1)**.The results showed that no statistically significant differences were found between studied groups as regards Age, sex and duration of CKD.

**Table (2) :** shows comparison between group A and group B regarding catheter site, dwell time of catheter insertion, number of catheters, time from catheter removal, frequency of catheter infection and acetyl salicylic acid use; where, regarding catheter site, statistically significant increase of CVS among patients with subclavian catheters was found. ($x^2$ = 3.93, p<0.05, relative risk factor **(RR)** =1.81 and 95% CI [1.18-2.76] ), Statistically highly significant increase of CVS in group A than group B regarding dwell time of catheter insertion was found, ($x^2$ = 36.68, p<0.001, **RR** =4.03 and 95% CI [2.39-6.8] ). Highly significant increase of CVS regarding the number of catheters insertion in one site, ($x^2$ = 82.92, p<0.001, **RR** =5.58 and 95% CI [3.8-8.19] ).

Regarding time from catheter removal ( days) between studied groups, table(2) shows a statistically significant difference, ($x^2$ =9.75, p=0.0017, **RR** =1.36 and 95% CI [1.14-1.62] ) and shows highly significant difference between group A and group B as regard to frequency of catheter infection which was more in group A. ($x^2$ =70.59, p<0.001, **RR** =5 and 95% CI [3.38-7.4] ).

Finally, table(2) shows highly statistically significant difference between group A and group B, regarding ASA consumption with significant increase of CVS with low ASA consumption, ($x^2$ =74.73, p<0.001, **RR** =2.86 and 95% CI [2.04-4] ).

Multiple regression analysis of variables in table (3) shows the only significant predictors that were significant to the model were catheter site [OR=2.01, 95%CI (1.1-3.7) and p=0.015], dwell time of catheter insertion [OR=2.56, 95%CI (1.39-4.74) and p=0.0011], and catheter number, [OR=2.79, 95%CI (1.51-5.16) and p<0.001].

**Table(1):demographic data and duration of CKD of the patients of the study.**

| Variable | Group A (with stenosis) (n = 64) | Group B (without stenosis) (n = 136) | T | P value |
|---|---|---|---|---|
| Age (years): | | | | |
| Mean ±SD | 40.7±13.9 | 42.2±14.2 | t = 0.47 | 0.63 |
| Range | 17-74 | 18-75 | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Sex: | | | | | | | |
| Male | 36 | (56.25%) | 74 | (54.4%) | $\chi^2$=0.06 | 0.8 | |
| Female | 28 | (43.75%) | 62 | (45.6%) | | | |
| Duration of CKD: | | | | | | | **RR (95%CI)** |
| ≤30 months | 34 | (53.1%) | 76 | (55.9%) | $\chi^2$= 0.08 | 0.78 | 1.06 |
| >30 months | 30 | (46.9%) | 60 | (44.1%) | | | (071-1.59) |

**S**: Significant ( p value < 0.05) **NS***: Non significant ( p value > 0.05) **HS**: Highly significant ( p value < 0.001)
CKD**:** chronic kidney disease

**Table (2) : Comparison between group A and group B regarding catheter site, dwell time of catheter insertion, number of catheters, time from catheter removal, frequency of catheter infection and ASA use.**

| **Variable** | **Group A (with stenosis)** | | **Group B (without stenosis)** | | **$x^2$** | **P** | **RR (95% CI)** |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | | | |
| **Catheter site**: | | | | | | | |
| Internal jugular | 24 | 37.5 | 80 | 58.8 | 7.93 | 0.004 | 1.81 (1.18-2.76) |
| Subclavian | 40 | 62.5 | 56 | 41.2 | | | |
| **Dwell time of insertion** : | | | | | | | |
| ≤ 25 days | 14 | 21.9 | 92 | 67.6 | 36.68 | <0.001 | 4.03 (2.39-6.8) |
| > 25 days | 50 | 78.1 | 44 | 32.4 | | | |
| **number of catheters:** | | | | | | | |
| ≤ 2 | 24 | 37.5 | 130 | 95.6 | 82.92 | <0.001 | 5.85 (3.8-8.19) |
| > 2 | 40 | 62.5 | 6 | 4.4 | | | |
| **Catheter removal Time** : | | | | | | | |
| ≤ 15 days | 52 | 81.25 | 80 | 58.8 | 9.75 | 0.0017 | 1.36 (1.14-1.62) |
| > 15 days | 12 | 18.75 | 56 | 41.2 | | | |
| **Catheter infection**: | | | | | | | |
| **-ve** | 24 | 37.5 | 126 | 92.65 | 70.59 | <0.001 | 5 (3.38-7.4) |
| **+ve** | 40 | 62.5 | 10 | 7.35 | | | |
| **ASA use:** | | | | | | | |
| **-ve** | 52 | 81.25 | 24 | 17.6 | 74.73 | <0.001 | 2.86 (2.04-4) |
| **+ve** | 12 | 18.75 | 112 | 82.4 | | | |

**S**: Significant ( p value < 0.05) **NS**: Non significant ( p value > 0.05) **HS**: Highly significant ( p value < 0.001)
**ASA**: acetylsalicylic acid

**Table (3) Multiple regression analysis of variables.**

| Variable | OR (95%CI) | P |
|---|---|---|
| **Catheter site** | 2.01 (1.1-3.7) | 0.015 (S) |
| **Dwell time of insertion** | 2.56 (1.39-4.74) | 0.0011 (S) |
| **Catheter number** | 2.79 (1.51-5.16) | < 0.001 (HS) |

**S**: Significant ( p value < 0.05) **NS**: Non significant ( p value > 0.05) **HS**: Highly significant ( p value < 0.001)

## DISCUSSION:

Central venous catheters are the most frequent causes of benign central vein stenosis, a potentially fatal complication for dialysis patients because they limit the efficiency and duration of native or prosthetic peripheral access routes and can cause malfunctioning of dialysis catheters and reduce the number of veins suitable for catheterization **(9).**

The development of CVS among the patients with history of central venous catheterization is likely related to mechanical injury from either catheter insertion or continuous catheter movement inside the vasculature, invoking endothelial damage, intimal hyperplasia, and fibrosis **(10).**

Patients undergoing hemodialysis need chronic vascular access to provide repeated access to the circulation with minimal complications. Complications associated with vascular access include stenosis, thrombosis, infection, digital ischemia, heart failure, pseudo aneurysm, and aneurysm **(11).**

Central venous cannulation can lead to the development of central venous stenosis. In patients on dialysis, this is primarily related to the placement of an ipsilateral central venous catheter but can also occur without a previous history of catheter placement. It is expected that central venous cannulation leads to intimal injury associated with focal endothelial denudation, increased smooth muscle cells and vein wall thickening **(12).**

In our study, we screened 200 hemodialysis patients from those attending to the dialysis units in Zagazig university hospitals & in health insurance hospital (Elmabarra). Those patients were classified into two major groups, group A (with stenosis) of 64 patients and group B (without stenosis) of 136 patients.

We found a prevalence of 32% of stenosis following catheterization of central vein in our study patients even in patient without past history of previous of catheter insertion. The previous results are matched with that of **MacRae,** who evaluated 235 patients, while 133 of them underwent venography for access related concerns over a 14 months period of these 133 patients, 55 (41%) had evidence of significant CVS (> 50% luminal obstruction) on venogram (**12)**.

We could not find any difference between the patients with and without stenosis regarding age and sex.

As regard to site of catheter, the number of patients who have internal Jugular catheter in group A (with stenosis), was 24 (37.5%) and the number of patients who have subclavian catheter was 40 (62.5%), while in group B (without stenosis) the number of patients who have Internal jugular catheter was 80 (58.8%) and the number patients who have subclavian catheter was 56 (41.2%) **(12).**

Statistically significant increase of CVS among patients with subclavian catheters than internal jagular catheters was found in our study. In agreement with our results, **Chesterton et al.,** proved that unexpected stenosis of the central veins occurs in 42% of hemodialysis patients in a study that evaluated 69 patients on hemodialysis most of then subclavian vein site **(13).**

As regard to duration of having CKD, no significant difference was found between group of patients with CVS, and group of patients without CVS. In agreement with our results, **Minoo et al.,** proved that, there was no significant difference between the patients with and without stenosis regarding duration of having CKD **(14).**

As regard to dwell time of catheter insertion, we found highly statistically significant increase of CVS with long dwell time of catheter insertion when comparing CVS group of patients with non-CVS group of patients.

In agreement with our results, **Stephen et al.,** stated that one of the most important risk factors that lead to central vein stenosis is the long duration of central vein catheter in patients on hemodialysis that may lead to endothelial injury, mechanical irritation, thickening of the vein wall, enhanced smooth muscle cell production and catheter attachment to the vessel wall with thrombus and collagen formation take place **(15).**

As regard to number of catheters, we found highly statistical significant increase of CVS with increase in number of catheter that had been placed in one site when comparing CVS group of patients with non-CVS group of patients.

In agreement with our results, **Oguzkurt et al.** stated that the more the catheters used in the same place, the more the liability of central vein stenosis **(1).** Also, **MacRae et al.,** proved that, in patients with any history of previous HD catheter insertion, multivariate analysis demonstrated that number of catheters remain a significant factor. They used patients who have history of catheter insertion for only one time, while we used patients in our study with history of 1-3 times catheter insertions in one site. As well as, they used patients who have longer duration of hemodialysis (43 ± 12 months), while we used patients in our study with duration of hemodialysis ranging from 2-70 months **(12).**

As regard to frequency of complications (infection), we found statistically high significant increase of CVS with occurrence of infection when comparing CVS group of patients with non-CVS group of patients ($p< 0.001$).

In agreement with our results, **Denis Frasca, et al., stated** that infection is a strong risk factor in occurrence of central vein stenosis **(16).**

Regarding the role of ASA consumption in minimizing the occurrence of central vein stenosis, we found statistically high significant increase of CVS with less use of ASA.

In agreement with our results, the study of **Yevzlin et al.,** proved that, consumption of (ASA) has a great and significant role in minimizing occurrence of platelet aggregation and thrombus formation then helps the normal blood flow around the catheter and eventually, this has a great role in prevention of central vein stenosis in most of patients on hemodialysis **(17).**

From the previous results of our study, we concluded that central vein stenosis is not a rare problem in patients on hemodialysis. The risk factors that may lead to central vein stenosis include, infection, thrombosis, recurrent use of the same place in order to put the catheter in and also the long duration of placement of the catheter, so all these factors are in need to be avoided in order to obtain normal blood flow and normal caliber of central vein. Finally, low dose ASA plays a great role in minimizing central vein stenosis as shown by the results of our study.

**Recommendation:**

Early creation of an arteriovenous access prior to initiating dialysis can reduce the need for central venous catheters and thus reduce the prevalence of central vein stenosis. Follow up of central venous catheters is needed continuously. We have to avoid or minimize the risk factors for CVS. ASA prior to central vein catheterization may play a great role in minimizing stenosis of central veins.

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