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## of Medical Research: F

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Prevalence of Diabetes Mellitus

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Highlights

Surgical Management for Pseudocyst

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Discovering Thoughts, Inventing Future

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Diseases
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# A New Method of Surgical Management for Pseudocyst of Pinna

By Professor Dr. Sudhangshu Kumar Ballav, Dr. Devnath Talukder, Dr. Shailendra Nath Biswas & Dr. Susmita Ballav

*Khulna City Medical College*

*Abstarct-* *Introduction:* Pseudocyst of pinna is not very common problem in ENT practice. This is a benign painless cystic swelling arising in pinna and visible on lateral surface of pinna. No obvious cause of this swelling can be identified. This is an intra cartilaginous cyst without any epithelial lining. So, the name pseudocyst. There is no definite and effective medical treatment for this pseudocyst. There are so many surgical treatments available. We describe a novel minimal surgical technique for this condition.

*Methods:* 24 patients 19 male and 5 female ages ranging from 25 -45 years were included in this trial. All patients were selected from ENT out patient department of Khulna Medical College Hospital and from my private consultancy Clinic between 1st January 2015 to 31st December 2018.

*Keywords:* *pinna, pseudocyst, new technique.*

*GJMR-F Classification:* *NLMC Code: QZ 200*


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# A New Method of Surgical Management for Pseudocyst of Pinna

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*Abstract-* *Introduction:* Pseudocyst of pinna is not very common problem in ENT practice. This is a benign painless cystic swelling arising in pinna and visible on lateral surface of pinna. No obvious cause of this swelling can be identified. This is an intra cartilaginous cyst without any epithelial lining. So, the name pseudocyst. There is no definite and effective medical treatment for this pseudocyst. There are so many surgical treatments available. We describe a novel minimal surgical technique for this condition.

*Methods:* 24 patients 19 male and 5 female ages ranging from 25 - 45 years were included in this trial. All patients were selected from ENT out patient department of Khulna Medical College Hospital and from my private consultancy Clinic between 1st January 2015 to 31st December 2018. With proper aseptic measure and under local anesthesia very small stab incision was given by no15 BP blade on most dependent part of the cyst and a ventilation tube made up of plastic tube of a butterfly needle inserted through the stab incision just like a grommet insertion on tympanic membrane. Both ends of the plastic tube was just heated by gas lighter and pressed on metallic smooth surface so that ends of the tube took a shape of grommet. These patients were followed up over 3 months.

*Results:* 22 patients had successful outcome. We observed complete resolution after 2 weeks. Patients were advised to restrict head bath to avoid water entry through the tube while the tube was in situ. 2 patients developed secondary infection which were controlled by broad spectrum antibiotics and got cured without any other complications.

*Conclusion:* The new technique of surgical management is very simple, inexpensive, and effective minimal surgical method of management for the pseudocyst of pinna.

*Keywords: pinna, pseudocyst, new technique.*

## I. Introduction

Pseudocyst of pinna is an idiopathic benign painless cystic swelling developed spontaneously on the lateral aspect pinna due to accumulation of fluid. It is an intra cartilaginous cyst without having any epithelial lining. The common sites of origin are cymba concha, scaphoid fossa and triangular fossa of the pinna(1). These lesions are also named as endochondral pseudocyst, intra cartilaginous cyst and benign idiopathic cystic chondromalacia (2).

Histologically these are intra cartilaginous cyst without having any epithelial lining hence it is called pseudocyst. The fluid inside the cyst is yellow or straw colored serous or viscous fluid containing glucose and protein(3). The lesions are mostly unilateral.

These are simple lesions sometimes incidentally found by close contact but difficult to manage either by medical or surgical procedure. Hence there are so many modalities of management described in literature. Whatever modality of treatment is applied the aim of treatment includes restoration and preservation of normal appearance of pinna and prevention of recurrence(3).

We describe our experience of management of these comparatively less common simple lesions of pinna by applying our new and minimal surgical technique.

## II. Materials and Methods

24 patients were diagnosed clinically as pseudocyst of pinna in my private consultation clinic between 1st January 2015 to 31st December 2018. The procedure to be done was explained to the patients and their written consent taken for enrolment in the study.

Diagnosis was made by clinical examination and confirmed byaseptic aspiration of non-purulent straw or yellow color fluid from the cyst during surgical procedure.

All patients were posted for our minimal invasive new technique of surgical intervention. With all aseptic precaution and under local anesthesia a stab incision was given on selected dependent part of the cyst and through that stab incision instantly made ear grommet type drain tube made up of butterfly needle set inserted. This self-retaining type of drain tubes were kept in situ for two weeks. After two weeks we observed complete resolution of the cyst. Then we removed the drain tube. The patients were followed up once in a month for 3 months to see any recurrence.

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## III. Results

Twenty-four patients were diagnosed as cases of pseudocyst of pinna from January 2015 to December 2018. The age distribution in our study group ranged from 25 to 45 years. The lesions were seen more in scaphoid fossa followed by triangular fossa and cymba concha. Twenty-two patients had complete resolution within two weeks. Two patients developed secondary infection which was effectively controlled by broad spectrum antibiotics and subsequently cured.

## IV. Discussion

The pseudocyst of pinna is fairly an uncommon problem found among adult and predominantly in males (79.16%) in our study group consistent with other reports. The sites of origin were scaphoid fossa, triangular fossa and cymba conchain order of precedence. The predisposing factors and etiology were not known. Its pathogenesis is hypothetical as yet. Hormonal factor may play a part for male predominance (4).

Abnormal release of lysosomal enzymes from chondrocytes give rise to progressive dilatation and formation of intra cartilaginous cavity (5). One hypothesis explained congenital embryonic dysplasia of the auricular cartilage that leads to formation of pseudocyst (6).

There is no single accepted method of treatment for this condition. The various modalities of treatment are close aspiration and pressure bandage, aspiration with buttoning, aspiration and intralesional corticosteroid injection, anterior wall deroofing, incision and curettage of cartilage wall, intralesional sclerosing agents etc. are being practiced (6) (7)(8). Fibrin glue as a sealing material between the two flaps of cartilage has been reported (9). Whatever method is applied to treatment there is every chance of recurrence in significant number of cases (10)(11).

## V. Conclusion

Almost in all methods of treatment required compression dressing which is difficult to provide and maintain. Our new technique of grommet type plastic tubedrainout insertion through a stab incision does not require any pressure dressing. Moreover, it is simple cost effective and compliant to patient with acceptable outcome.

## References Références Referencias


1. Choi S, Lam KH, Chan KW, Ghadially FN, Ng As. Endochondral pseudocyst of the auricle in Chinese. Arch Otolaryngol 1984; 110:792-6. (PUBMED)
2. Chen Q, Fei Y, Zho T, Luo D, Wu B, Yang X, et al. Research on the immunological cause of auricular pseudocyst. Lin Chuang Er Bi Yan Hou KeZhi 2001; 15: 304-5.
3. Schulte KW, Neumann NJ, Ruzicka T. Surgical pearl: The close-fitting ear cover cast-a noninvasive treatment for pseudocyst of the ear. J Am Acad Dermatol 2001; 44: 2856.
4. Bhat VS, Shipla, Nitha, Ks R. Deroofing of auricular pseudocyst: Our experience. J Clin Diagn Res 2014; 8: KC05-7.
5. Miyamoto H, Okajima M, Takahashi I. Lactate dehydrogenase isoenzymes and intralesional steroid injection therapy for pseudocyst of the auricle. Int J Dermatol2001; 40: 380-4.
6. Engel D. Pseudocysts of the auricle in Chinese. Arch Otolaryngol 1966;83:197-202(PUBMED).
7. Chang CH, Kuo WR, Lin CH, Wang LF, Ho KY, Tsai KB, et al. Deroofing surgical treatment for pseudocyst of the auricle J Otolaryngol 2004; 33: 177-80.
8. Tuncer S, Basterzi Y, Yavuzer R. Reccurrent auricular pseudocyst: a new treatment recommendation with currettage and fibrin glue. Dermatol Surg 2003: 29; 1080-3.
9. Rehman A, Sangoo m, Hamid S, Wani A, Khan N. Recurrent pseudocyst pinna: A rational approach to treatment. Int J Sci Res Publ 2013; 3:1-4.
10. Ramadass T, Ayyaswamy G. Pseudocyst of auricle etiopathogenesis, treatment update and literature review. Indian J Otolaryngol Head Neck Surg. 2006; 58:156-9(PMC free article) (PubMed) (Google Scholar).
11. Lim CM, Goh YH, Chao SS, Lynee L. Pseudocyst of the auricle. Laryngoscope. 2002; 112: 2033-6. (PubMed) (Google Scholar).


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*Fig-1*



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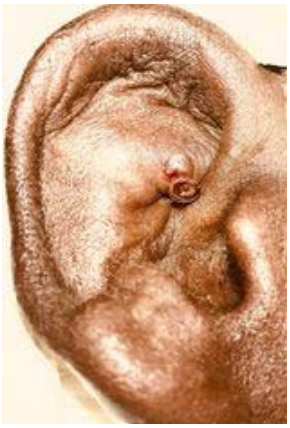

Fig-2



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# The Functional Outcome of Normal or High Blood Pressure in Patients with Chronic Glomerulonephritis and Nephrotic Syndrome is Dependent on Association with Functional, Histologic and, Proteinuric Parameters

By Claudio Bazzi

*Abstarct- Background:* Normal (BP0)or high blood pressure (BP1)are variably present in patients with chronic glomerulonephritis (GN) and Nephrotic Syndrome (NS). At biopsy each BP0 or BP1 patient is associated with different values of renal function, urinary proteins excretion and renal lesions severity [GGS%, TID and AH score]. Thus outcome of BP0 and BP1 may be dependent inevry patient on the associations with these parameters and by eventual treatments with immunosuppressive agents.

*Methods:* In 151 patients with GN and NS the outcome was evaluated in BP0 and BP1 patients according to eGFR≥ or <60 ml/min/1.73 m2. In 140 patients with renal biopsy performed at the same time of all parameters the outcome was evaluated for 3 types of renal lesions severity (GGS%, TID score and AH score) and according to 4 groups of combined urinary excretion of IgG/C and α2m/C. The treatment with steroids and cyclophosphamide was evaluated.

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# The Functional Outcome of Normal or High Blood Pressure in Patients with Chronic Glomerulonephritis and Nephrotic Syndrome is Dependent on Association with Functional, Histologic and, Proteinuric Parameters

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*Methods:* In 151 patients with GN and NS the outcome was evaluated in BP0 and BP1 patients according to eGFR ≥ or <60 ml/min/1.73 m2. In 140 patients with renal biopsy performed at the same time of all parameters the outcome was evaluated for 3 types of renal lesions severity (GGS%, TID score and AH score) and according to 4 groups of combined urinary excretion of IgG/C and α2m/C. The treatment with steroids and cyclophosphamide was evaluated.

*Aim of study:* Identify which functional, proteinuric. histologic and therapeutic factors in combination with BP0 and BP1 are associated with outcome improvement or worsening.

*Results:* In BP 0 patients the highest rate of "Remission & persistent NRF ("No progr") is 100% observed in BP0 patients associated with IgG/C&α2m/C group 0+0 and treated with Steroids and Cyclophosphamide. The percentages of "noprogr" of the other parameters were: TID score 0 (96%), AH score 0 (87.5%), eGFR ≥ 60 ml/min (84%).In BP 1 the worse rate of "Progression & progression risk" ("progr") is 100% observed in BP1 patients associated with IgG/C&α2m/C group 1+1 and treated with Steroids and Cyclophosphamide; the "progr" percentages of the other parameters were: TID score 4-6 (96%), AH score 2-3 (96%), IgG/C &α2m/C group 1+1 (85%), eGFR< 60 ml/min (82%).

*Conclusions:* The outcome in BP0 and BP1 patients is dependent on their association with some parameters: renal function, renal lesions severity and some proteinuric parameters alone or in combination.

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## I. Introduction

The clinical significance of arterial hypertension in renal diseases has been evaluated in several studies (1-12). In a cohort of 151 patients with chronic glomerulonephritis (GN) and nephrotic syndrome (NS) normal (BP 0) and high blood pressure (BP 1) are present with variable percentage according to several factors: eGFR ≥ or < 60 ml /min73.1 m2; GGS: 0% vs ≥ 20%; TID score 0 vs 4-6; AH score 0 vs 2-3, TUP/C <vs≥ median and combined excretion of IgG/C and α2m/C groups (for these groups definition see later in Laboratory analysis Section).The combination of each patient with one or more functional, histologic and proteinuric parameters and eventual treatment with Steroids and Cyclophosphamide is associated with different percentages of favourable outcome (Remission and PNS with long lasting NRF": briefly defined "noprogr.") or unfavourable outcome (ESRD & eGFR< 50% of baseline & PNS with CRF: briefly defined "progr"). Aim of the study: assess how high blood pressure increases according to lower values of eGFR and increased values of the main histological parameters such as Global Glomerular Sclerosis (GGS%), extent of tubulo-interstitial damage (TID score) and Arteriolar Hyalinosis (AH score) and how functional outcome may improve or worse according with the association with these functional, proteinuric and histologic parameters.

## II. Patients and Methods

The patients cohort included in the study was not selected. The patients attending the Nephrology and Dialysis Unit of San Carlo Borromeo Hospital, Milan, Italy, between January 1992 and April 2006 with renal biopsy diagnosis of GN with NS were 204; 26 patients with acute reversible renal failure (ARF) at biopsy were excluded from analysis as do not meet the inclusion criterion (chronic glomerulonephritis). The 151 have functional outcome and 84 of them were selected for treatment with Steroids and Cyclophosphamide. The diagnosis of all 151 patients were: Crescentic IgAN



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(CIgAN) n. 12, Focal Segmental Glomerulosclerosis (FSGS, n. 32), IgAN (2), Idiopathic Membranous Nephropathy (IMN, n. 66), Minimal change disease (MCD, n. 11), Membrano-proliferative glomerulonephritis (MPGN, n. 15): Lupus Nephritis [LN, n. 13: (WHO LN classes: 4: n. 11; 5 n. 2)].Inclusion criteria: nephrotic syndrome (proteinuria ≥3.5 g/24h and/or serum albumin <3.0 g/dL); at least six glomeruli in renal biopsy; typical features at light and immunofluorescence microscopy; no clinical signs of secondary GN except for LN. The functional outcome was evaluated in all 151 patients with rather long follow up[mean 91±77 months, (2-311].Five types of outcome were considered: 1) Remission of NS: complete: proteinuria ≤ 0.30 g/24h; partial: proteinuria ≤ 2.0 g/24h; 2) persistent NS with long lasting normal renal function (PNS NRF) after a follow up of 91±73 months (30-200); 3) progression to end-stage renal disease (ESRD); 4) eGFR reduction ≤ 50% of baseline; 5) persistent NS with chronic renal failure (CRF) and progressive eGFR reduction (from 49.3 to 39.1 ml/min/1,72 m2).Usually in prediction studies the outcomes considered are Remission and ESRD. We decided to evaluate not only each type of outcome considered alone but the combination of outcomes with similar prognostic significance: thus Remission was evaluated in combination with persistent PNS with long lasting NRF, afterwards indicated as ""noprog."; ESRD and eGFR≤ 50% were evaluated in combination with persistent PNS with CRF characterized by eGFR reduction from 49.3 to 39.1 ml/min/1,72 m2 and thus candidate for progression to ESRD, afterwards indicated as "progr".

## III. Laboratory Analysis

Proteinuria was measured in 24 hour urine collection and second morning urine sample by the Coomassie blue method (modified with sodium-dodecyl-sulphate) and expressed as 24/hour proteinuria and protein creatinine/ratio (mg urinary protein/g urinary creatinine). Serum α and urinary creatinine were measured enzymatically and expressed in mg/dL. Serum albumin and IgG and urinary IgG, α2-macroglobulin (α2m), Albumin and α1-microglobulin (α1m) were measured by immunonephelometry; urinary proteins were expressed as urinary protein/creatinine ratio (IgG/C, α2m/C, Alb/C, α1m/C). Estimated glomerular filtration rate (eGFR) was measured by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula (13). Three types of renal lesions that are markers of disease severity in any type of GN were evaluated: percentage of glomeruli with global glomerulosclerosis (GGS%); extent of tubulo-interstitial damage (TID) evaluated semi-quantitatively by a score: tubular atrophy, interstitial fibrosis and inflammatory cell infiltration graded 0, 1 or 2 if absent, focal or diffuse (TID global score: 0-6); extent of Arteriolar Hyalinosis (AH) evaluated semiquantitatively by a score: 0, 1, 2, 3 if absent, focal, diffuse, diffuse with lumen reduction, respectively (AH global score 0-4). In our recent study (14)in151 patients with GN and NS, were calculated the median of IgG/C (IgG/C 0<median and IgG/C1>median); the median of α2m/C was calculated independently in IgG/C 1 and IgG/C 0 patients, respectively and defined α2m/C 0 and α2m/C 1 if < or > the median. On the basis of combination of IgG/C and α2m/C medians were defined 4 groups: IgG/C 1 & α2m/C 1, IgG/C 1 & α2m/C 0, IgG/C 0 & α2m/C 1, IgG/C 0 & α2m/C 0) more briefly defined (1+1, 1+0, 0+1, 0+0). These groups assess disease severity of all patients: moreover the combination of BP 1 with (1+1) group and BP 0 in combination with (0+0) group predict 100% of "progr" and 100% of "noprogr" respectively (Table 3).

## IV. Statistical Analysis

Continuous variables are expressed as means±SD. Categorical variables are expressed as the number of patients (%). The differences of mean were determined by t-test; categorical variables by the chi-square test. All statistical analyses were performed using Stata 15.1 (StataCorp LP, TX, USA). Two-sided $p<0.05$ was considered statistically significant.

## V. Results

The functional outcome has been evaluated according to the highest and lowest values of eGFR (≥vs< 60 ml/min), GGS 0% vs ≥ 20%, TID score 0 vs 4-6 and AH score 0 vs 2-3. The outcome was classified as "noprog" (remission and persistent NS with long lasting normal renal function) and "progr" (ESRD, eGFR< 50% of baseline and persistent NS with CRF). In general the patients with more severity of renal function and histological parameters show an increase of percentage of patients with high blood pressure, while the patients with eGFR ≥ 60 ml/min, GGS 0%, TID score 0 and AH score 0 usually show an increase of patients with normal blood pressure. The functional outcome was also evaluated according to groups of combined urinary excretion of IgG/C & α2m/C (0+0, 0+1, 1+0, 1+1).

*Outcome in BP 0 and BP 1 patients according to level of renal function eGFR ≥ or < 60 ml/min.*

In all the 151 patients with GN and NS 61 patients (40%) have normal blood pressure (BP 0) and 90 patients (60%) have high blood pressure (BP 1); In 61 BP 0 patients "No progr" is 80% and "Progr." 20%; in 90 BP 1 patients "no progr." 42% and "progr." is 58% (Table 2). BP 0 and BP 1 are highly significant different for baseline and last eGFR, IgG/C, α1m/C, GGS%, TID score and AH score (Table 1).

In eGFR ≥ 60 ml/min/1.73 m2 the patients are 97: BP 0 n. 57 (59%) and BP 1 n. 40 (41%); in BP 0 "no

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progr" is 82% and "progr" 18%;in 40 patients BP 1 "noprogr " is 72.5% and "progr" 27.5%. In eGFR< 60 ml/min the patients are 54: BP 0 are n. 4 (7%) and BP 1 are n. 50 (93%); in the 4 BP 0 "noprogr" is 25% and "progr" 75%;in the 50 patients BP 1 "no progr" is 18% and " Progr" is 82% (Table 2).

*Outcome in BP0 and BP1 patients according to percentages of global glomerular sclerosis (GGS 0% versus GGS ≥ 20%).*

The patients with GGS 0% (n. 53) were compared with patients with GGS ≥20% (n. 34). In patients with GGS 0% (n.53) the BP 0 are 34 (64%) and BP1 19 (36%); the 34 BP0 show 85% of "noprogr" and 15 % progr". The 19 BP1show: 15 (79%) of "noprogr" and 4 (21%) of "progr". In patients with GGS≥ 20% (n. 34) the BP 0 are 2(6%) and BP1 are 32 (94%); the 2 BP0 show 1 "noprogr" (50%) and 1 "progr" (50%); the 25 BP1 patients show 78% of "noprogr" and (22%) of "progr".

*Outcome in BP0 and BP1 patients according to value of TID score [0 (absent) versus tubular atrophy, interstitial fibrosis and inflammatory cell infiltration diffuse (score 4-6)].*

The patients with absent tubulo-interstitial damage (TID score: 0, n. 39) were compared with patients with focal or diffuse tubular atrophy, interstitial fibrosis and inflammatory cell infiltration (TID score: 4-6, n. 27). In patients with TID 0 the BP 0 are 24 (62%) and BP1 15 (38%); the 24 BP0 show 96% of "noprogr" and 4% of "progr" ; the 15 BP1show 53% of "noprogr" and 47% of "progr". In patients with TID score 4-6 BP 0 are 2 (7%) and the BP 1 are 25 (93%): the BP 0 Show 0% of "noprogr" (0%) and 1(100%) of "progr"; the BP1 show 4% of "no progr" and 96% of "progr". Thus the functional outcomes are rather different as in the BP1 patients with TID score 0 "progr" is 47%, while in BP1 patients with TID score 4-6 the "progr" is 96%.

*Outcome in BP0 and BP1 patients according to value of AH (arteriolar hyalinosis) absent (0) and arteriolar hyalinosis diffuse (2) and diffuse with lumen reduction (3).*

In patients with AH score 0 the patients are n. 86 with BP 0 is n.48 (56%) and BP 1 n. 38 (44%): the 48 BP 0 patients show 41 (85%) of "no progr" and 7 (15%) of "Progr". In patients with BP 1 (n.38) "noprogr" is 22 (58%) and "progr" is 16 (42%).

In patients with AH score 2-3 (2: diffuse arteriolar hyalinosis, 3: diffuse arteriolar hyalinosis with lumen reduction) BP 0 are2 (outcome not valuable); the BP1 patients are n. 14: "noprogr" n. 2 (14%) and "Progr." n. 12 (86%).

*Outcome in BP 0 and BP 1 patients according to the groups of combined urinary excretion of IgG/C & α2m/C (0+0, 0+1, 1+0, 1+1).*

The 0+0 group in combination with BP0 and with Steroids and Cyclophosohamide treatment (n. 15 patients) show 100% of "noprogr" and 0% of "progr". The 1+1 group in combination with BP1 and Steroids and Cyclophosphamide treatment (n. 14 patients) "noprogr" is 0% and "progr." is 100%.

In the groups 0+1 and 1+0 (n. 55 patients) treated with Steroids and Cyclophosphamide "noprogr" are 32 patients (58%) and "progr" are 23 (42%).

## VI. Discussion

In 151 patients with GN and NS the percentage of normal blood pressure (BP 0) is lower [n. 61 (40%)] than that of high blood pressure (BP 1) [n. 90 (60%)]. The percentages of BP 0 and BP 1 are influenced by level of renal function (eGFR ≥ or < 60 ml/min) with increase of percentages of BP 0 in patients with eGFR ≥ 60 ml/min (59%) and increase of percentages of BP 1 (93%) in patients with eGFR< 60 ml/min. These variations in percentages of BP 0 and BP 1 changes the outcome: "noprogr" is reduced from 42% to 18% in BP 1 patients associated with eGFR< 60 ml/min and "progr" increases from 58% to 82% in BP 0 associated with eGFR ≥ 60ml/min. Similar observations by comparison of GGS 0% with GGS ≥ 20% that show a reduction of "noprogr" from 42% to 22% and increases the percentage of "progr" from 58% to 78%. Similar observations evaluating TID score and AH score. These data show that the functional outcome in BP 0 and BP 1 is dependent on association with functional, proteinuric and histologic parameters. This observation allow to suggest that the combination in evry patient of BP with eGFR, GGS%, TID score and AH score may be a predictor functional outcome at diagnosis (for example prediction of ESRD) and this prediction may influence the choice of treatment.

## VII. Conclusions

Considering only the percentage of normal blood pressure (BP 0, n. 61) and high blood pressure (BP 1, n 90) as such in 151 patients with GN and NS the BP 0 patients show better outcome: "noprog." 80%and "Progr." 20%, while in BP 1 patients "no Progr." is 42% and "Progr" 58%. The highest percentage of "noprogr" are observed in BP 0 associated with eGFR ≥ 60 ml/min ("noprogr" 82%), GGS 0% ("noprogr" 85%), TID score 0 ("noprogr" 96%) and AH score 0 ("noprogr" 85%). The highest percentages of "progr" are observed in BP1 patients associated with eGFR<60 ml/min ("progr" 82%), TID score 4-6 ("progr" 96%) and AH score 2-3 ("progr" 86%). Thus the most powerful parameters associated with worse renal function are eGFR<60, TID score 4-6 and AH score 2-3. These results show that outcome of BP 0 and BP 1 patients are associated with eGFR<vs ≥ 60 ml/min, TID score 0 vs 4 -6 and AH score 0 vs 2-3. In evry single patients the combination



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at diagnosis of these 4 parameters may be able to predict the functional outcome and suggest that patients whose combination predict ESRD should not treated with immunosuppression.

*Table 1:* Baseline clinical, functional, proteinuric and histologic parameters in 151 patients with glomerulonephritis (GN) and nephrotic syndrome (NS) 61 with baseline normal blood pressure (BP 0) and 90 with high blood pressure (BP 1)

| | Normal BP (BP 0) n. 61 (40%) <140/90 mmHg | High BP (BP 1) n. 90 (60%) ≥ 140/90 mmHG | P |
|---|---|---|---|
| Age yrs | 38.4± 16.5 | 43.6±18.1 | |
| eGFR baseline | 94.3 ± 22.4 | 57.1 ±28.9 | <0.0001 |
| eGFR last | 75.2 ±33.4 | 39.8± 32.5 | <0.0001 |
| eGFRbasel. ≥ 60 | n. 57 | n. 40 | |
| eGFRbasel. < 60 | n. 4 | n. 50 | |
| TUP/C | 4086± 2731 | 5018± 3375 | 0.06 |
| IgG/C | 142± 140 | 296± 335 | 0.0001 |
| α2m/C | 6.64± 16.50 | 11.64± 16.76 | 0.07 |
| Alb/C | 3469±2397 | 4089± 2563 | 0.13 |
| α1m/C | 28.9±26.8 | 59.4 ± 47.6 | <0.0001 |
| GGS% | 4.7±8.2 | 17.0± 17.7 | <0.0001 |
| TID score | 1.01±1.18 | 2.48±1.76 | <0.0001 |
| AH score | 0.19±0.44 | 0.76±0.85 | < 0.0001 |
| IgG/C &α2mC 0+0 | 26 (43%) | 12 (13%) | |
| IgG/C &α2m/C 0+1 | 12 (20%) | 25 (28%) | |
| IgG/C &α2m/C 1+0 | 11 (18%) | 27 (30%) | |
| IgG/C &α2m/C 1+1 | 12 (20%) | 26 (29%) | |

*Table 2:* Outcome according to the functional parameter eGFR ≥ vs<60 ml/min in patients with BP0 and BP1

| | | Remission & PNS NRF "no progr" | ESRD & eGFR<50% & PNS CRF "Progr" |
|---|---|---|---|
| All pts BP n.151 | | | |
| All ptsBP 0 | BP 0 n. 61 (40%) | 80% | 20% |
| All pts BP 1 | BP 1 n. 90 (60%) | 42% | 58% |
| | | | |
| eGFR ≥60 all BP 97 | BP0 n. 57 (59%) | 82% | 18% |
| eGFR ≥60 all BP 97 | BP1 n. 40 (41%) | 72.5% | 27.5 |
| | | | |
| eGFR<60 all BP 54 | BP0 n. 4 (7%) | 25% | 75% |
| eGFR<60 all BP 54 | BP1 n. 50 (93%) | 18% | 82% |



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*Table 3:* Outcome according to histologic parameters: GGS 0% vs ≥20%, TID score 0 vs 4-6. AH score 0 vs 2-3 in in patients with BP0 and BP 1

| Histologic parameters | | Remission & PNS NRF "no Progr" | ESRD & eGFR<50% & PNS CRF "Progr" |
|---|---|---|---|
| GGS 0% all BP 53 | BP0 n. 34 (64%) | 85% | 15% |
| GGS 0% all BP 53 | BP1 n. 19 (36%) | 79% | 21% |
| | | | |
| GGS≥20% all BP 34 | BP0 n. 2 ( 6%) | 50% | 50% |
| GGS≥20% all BP 34 | BP1 n. 32 (94%) | 22% | 78% |
| | | | |
| | | | |
| TID sc. 0 all BP 39 | BP0 n. 24 (62%) | 96% | 4% |
| TID sc. 0 all BP 39 | BP1 n. 15 (38%) | 53% | 47% |
| | | | |
| TID sc.4-6 all BP 27 | BP0 n. 2 ( 7%) | Not valuable | Not valuable |
| TID sc.4-6 all BP 27 | BP1 n. 5 (93%) | 4% | 96% |
| | | | |
| | | | |
| AH score0 all BP 86 | BP0 n. 48(56%) | 85 % | 15% |
| AH score0 all BP 86 | BP1 n. 38 (44%) | 58% | 42% |
| | | | |
| AH sc. 2-3 all BP 15 | BP0 n. 1( 7%) | Not valuable | Not valuable |
| AH sc. 2-3 all BP 15 | BP 1 n. 14(93%) | 14% | 86% |

*Table 4:* Functional outcomein 84 patients treated with Steroids and Cyclophosphamide according to the 4 groups of combined IgG/C & α2m/C excretion (1+1, 1+0, 0+1, 0+0) in combination with BP 1 and BP 0

| | IgG/C1&α2m/C 1 & BP 1 n. 14 | IgG/C1 & α2m/C1 n. 7 | IgG/C 1& α2m/C 0 n. 21 | IgG/C 0& α2m/C 1 n. 21 | IgG/C 0 & α2m/C 0 n. 6 | IgG/C 0&α2m/C 0 & BP 0 n. 15 | IgG/C 1&α2m/C 1 vs IgG/C 0& α2m/C 0 p |
|---|---|---|---|---|---|---|---|
| Age yrs | 46±20 | 42±18 | 37±18 | 38±16 | 41±19 | 37±18 | 0.83 |
| eGFR baseline | 31.2±19.1 | 46.0±29.9 | 74.1±27.4 | 67.1±26.6 | 97.9±25.3 | 105.9±22.4 | <0.0001 |
| Follow up months | 66±72 | 68±70 | 96±79 | 85±85 | 117±76 | 114±67 | 0.03 |
| TUP/C | 5933±2125 | 5795±2043 | 7373±4406 | 3781±2223 | 3194±2423 | 3543±2683 | 0.0005 |
| IgG/C | 448±196 | 434±181 | 101±148 | 112±41 | 63±32 | 53±31 | <0.0001 |
| α2m/C | 24.97±13.3 | 26.64±23.0 | 6.00±4.34 | 6.76±7.65 | 0.12±0.54 | 0±0 | <0.0001 |
| Alb/C | 4823±1645 | 4639±1676 | 3376±5982 | 3310±1975 | 3258±2592 | 3408±2881 | 0.02 |
| α1m/C | 91.6±37.3 | 79.4±45.3 | 56.2±29.3 | 37.9±20.8 | 18.8±10.4 | 19.2±10.8 | <0.0001 |
| GGS 0% | | 2 | | | 11 | | |
| TID score 0 | | 0 | | | 10 | | |
| AH score 0 | | 3 | | | 17 | | |
| BP 1 | 100% | 14 (67%) | | | 6 (29%) | 0% | |
| Rem.PNS NRF "noprogr" | 0 (0%) | (19%) | (48%) | (62%) | 34 (89%) | (100%) | |
| ESRD+PNSCRF+eGFR≤ 50% "Progr" | 14 (100%) | (81%) | (52%) | (38%) | 1 (4%) | (0%) | |



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## References Références Referencias


1. Chun-Gyoolhm, Hypertension in Chronic Glomerulonephritis. Electrolyte Blood Press. 2015 Dec; 13(2): 41–45. doi: 10.5049/EBP.2015.13.2.41
2. Bazzi C, Seccia TM, Napodano P, Campi C, Caroccia B, Cattarin L, and Calò LA,*High Blood Pressure Is Associated with Tubulointerstitial Damage along with Glomerular Damage in Glomerulonephritis. A large Cohort Study
3. Seccia T.M., Caroccia B., Calò L.A. Hypertensivenephropathy. Moving from classic to emerging pathogenetic mechanisms.J. Hypertens. 2017; 35: 205–212. doi: 10.1097/HJH.0000000000001170
4. Williams B., Mancia G., Spiering W., Agabiti Rosei E., Azizi M., Burnier M., Clement D.L., Coca A., de Simone G., Dominiczak A., et al. D.I.A.F.M. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J. Hypertens. 2018; 36: 1953–2041. doi: 10.1097/HJH.0000000000001940.5
5. de la Sierra A., Segura J., Banegas J.R., Gorostidi M., de la Cruz J.J., Armario P., Oliveras A., Ruilope L.M. Clinical features of 8295 patients with resistant hypertension classified on the basis of ambulatory blood pressure monitoring. Hypertension (Dallas, Tex. 1979) 2011; 57: 898–902. doi: 10.1161/HYPERTENSIONAHA.110.168948.
6. Parikh N.I., Hwang S.-J., Larson M.G., Meigs J.B., Levy D., Fox C.S. Cardiovascular Disease Risk Factors in Chronic Kidney Disease. Arch. Intern. Med. 2006; 166: 1884. doi: 10.1001/archinte.166.17.1884.8.
7. Alencar de Pinho N., Levin A., Fukagawa M., Hoy W.E., Pecoits-Filho R., Reichel H., Robinson B., Kitiyakara C., Wang J., Eckardt K.-U., et al. Considerable international variation exists in blood pressure control and antihypertensive prescription patterns in chronic kidney disease. Kidney Int. 2019; 96: 983–994. doi: 10.1016/j.kint.2019.04.032.
8. Yu Z., Rebholz C.M., Wong E., Chen Y., Matsushita K., Coresh J., Grams M.E. Association Between Hypertension and Kidney Function Decline: The Atherosclerosis Risk in Communities (ARIC) Study. Am. J. Kidney Dis. 2019; 74: 310–319. doi: 10.1053/j.ajkd.2019.02.015.
9. Muntner P., Anderson A., Charleston J., Chen Z., Ford V., Makos G., O'Connor A., Perumal K., Rahman M., Steigerwalt S., et al. Hypertension awareness, treatment, and control in adults with CKD: Results from the Chronic Renal Insufficiency Cohort (CRIC) Study. Am. J. Kidney Dis. 2010; 55: 441–451. doi: 10.1053/j.ajkd.2009.09.014. [11. Agarwal R. Caring for individuals with hypertension in CKD, especially those with low education.Kidney Int. 2019; 96: 820–822. doi: 10.1016/j.kint.2019.06.009.
10. Malhotra R., Craven T., Ambrosius W.T., Killeen A.A., Haley W.E., Cheung A.K., Chonchol M., Sarnak M., Parikh C.R., Shlipak M.G., et al. Effects of Intensive Blood Pressure Lowering on Kidney Tubule Injury in CKD: A Longitudinal Subgroup Analysis in SPRINT. Am. J. Kidney Dis. 2019; 73: 21–30. doi: 10.1053/j.ajkd.2018.07.015.]
11. Ikee R., Kobayashi S., Saigusa T., Namikoshi T., Yamada M., Hemmi N., Imakiire T., Kikuchi Y., Suzuki S., Miura S. Impact of Hypertension and Hypertension-Related Vascular Lesions in IgA Nephropathy. Hypertens Res. 2006; 29: 15–22. doi: 10.1291/hypres.29.
12. Haruhara K., Tsuboi N., Koike K., Kanzaki G., Okabayashi Y., Miyazaki Y., Kawamura T., Ogura M., Yokoo T. Ambulatory blood pressure and tubulointerstitial injury in patients with IgA nephropathy. Clin. Kidney J. 2015; 8: 716–721. doi: 10.1093/ckj/sfv083.
13. Levey A.S., Stevens L.A., Schmid C.H., Zhang Y.L., Castro A.F., Feldman H.I., Kusek J.W., Eggers P., Van Lente F., Greene T., et al. A new equation to estimate glomerular filtration rate. Ann. Intern. Med. 2009; 150: 604–612. doi: 10.7326/0003-4819-150-9-200905050-00006.
14. Bazzi C. and Nangaku M.Combined Urinary Excretion of IgG and α2-macroglobulin Very Simple Marker to Assess Disease Severity, Outcome Prediction and Responsiveness to Steroids and Cyclophosphamide in Patients with Chronic Glomerulonephritis and Nephrotic Syndrome.HSOA Journal of Nephrology & Renal Therapy 2021, 7:055; DOI 10.24966/NRT-7313/100055.




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# An Unusual Manifestation of Hughes-Stovin Syndrome- Case Report

By Monica Pon, Heng Man Lai, Chi Kun Mok, Hio Wai Ieong, Ka Pou Mok & Hou Ng

*Abstarct-* Hughes–Stovin syndrome (HSS) is very rare systemic disorder characterized by the combination of widespread vascular thrombosis and pulmonary vasculitis with serious morbidity and mortality. The exact etiology and pathogenesis of Hughes-Stovin syndrome is unknown. The clinical presentation of Hughes-Stovin syndrome includes hemoptysis, cough, dyspnea, fever and chest pain. Nearly 25% of patients with Hughes-Stovin syndrome develop vascular thromboembolism, arterial aneurysms, and arterial and venous occlusions with nonspecific vasculitis. The vascular lesion was most common in both artery and vein (68%), followed by vein (25%) and artery (8%). We report a case of a 56-years-old male patient presenting with fever of unknown origin. During the diagnostic work up, incidentally found aneurysm formation and thrombosis in the left upper lobe pulmonary artery segmental branch, thrombosis of the right lower lobe pulmonary artery segmental branches.

*Keywords: hughes-stovin syndrome, pulmonary artery aneurysm, hemoptysis, fever of unknow origin.*

*GJMR-F Classification: NLMC Code: WD 305*


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# An Unusual Manifestation of Hughes-Stovin Syndrome- Case Report

Monica Pon [α], Heng Man Lai [σ], Chi Kun Mok [ρ], Hio Wai Ieong [ω], Ka Pou Mok [¥] & Hou Ng [§]

*Abstract-* Hughes–Stovin syndrome (HSS) is very rare systemic disorder characterized by the combination of widespread vascular thrombosis and pulmonary vasculitis with serious morbidity and mortality. The exact etiology and pathogenesis of Hughes-Stovin syndrome is unknown. The clinical presentation of Hughes-Stovin syndrome includes hemoptysis, cough, dyspnea, fever and chest pain. Nearly 25% of patients with Hughes-Stovin syndrome develop vascular thromboembolism, arterial aneurysms, and arterial and venous occlusions with nonspecific vasculitis. The vascular lesion was most common in both artery and vein (68%), followed by vein (25%) and artery (8%). We report a case of a 56-years-old male patient presenting with fever of unknown origin. During the diagnostic work up, incidentally found aneurysm formation and thrombosis in the left upper lobe pulmonary artery segmental branch, thrombosis of the right lower lobe pulmonary artery segmental branches. He was diagnosed Hughes Stovin syndrome after excluding Behçet disease or any other autoimmune disease. He received methylprednisolone pulses followed by oral prednisolone and monthly intravenous cyclophosphamide. We repeated CT pulmonary angiogram after six months of treatment that showed stability of the pulmonary lesions. Unfortunately patient decided to stop treatment and after one month was admitted in our Emergency Department with massive hemoptysis that caused his death.

*Keywords: hughes-stovin syndrome, pulmonary artery aneurysm, hemoptysis, fever of unknow origin.*

## I. Introduction

Hughes–Stovin syndrome (HSS) is very rare disorder characterized by the combination of multiple pulmonary artery aneurysms and deep vein thrombosis. Less than 60 cases of HSS have been described in PubMed. The etiology and pathogenesis of Hughes-Stovin syndrome is still uncertain. It usually affects the young adult population and holds a predilection for the male gender. In a critical analysis published in 2021 by the HSS International Study Group, in which they included 57 cases, 43 (75%) were males, with a mean age of 33.8 years and mean disease duration of 54.2 months.

## II. Case Presentation

We present a case of a56-years-oldgentleman who suffered formal pha-thalassemia and type 2 diabetes mellitus well controlled on insulin therapy. He was admitted several times in the last two consecutive due to recurrent fever. His first admission was in January 2018. At that time he only presented fever of 38C and pneumonia was found on diagnostic work-up. After antibiotherapy he improved and was discharged. The second episode occurred in February 2019 that was managed in another hospital and no details were given. In March 2020 fever recurred again – maximum 38 – 39C and he was admitted in our Internal Medicine ward. He had ingested raw fish and clonorchissinensis ova were found in his stool culture. He was given praziquantel and discharged upon clinical improvement. After two weeks, he consulted our Emergency Department due to fever again. Blood test showed leukocytosis and C-reactive protein elevation. Blood cultures were sterile. There were fibronodular lesion and small patch lesions in bilateral lung in chest CT scan, considered as previous inflammatory sequelae. He was given broad spectrum antibiotics (meropenem and linezolid) and fever subsided. As he kept a febrile for over one week and as symptomatic, he was discharged.

One month after discharge fever recurred again. On physical examination in our Emergency Department, patient was alert, oriented, cooperative, febrile(39 C), tachycardic, hemodynamically stable, no skin rash or ulcer on the oral and genital mucosa, no palpable peripheral lymph node, cardiopulmonary auscultation was normal, on abdominal palpation there was mild tenderness on right upper quadrant without muscle guarding or rebound tenderness. No joint swelling or edema was noted. Neurological examination was normal. In the initial laboratory investigation, complete blood count showed Hb 10.2g/dL, normochromic and normocytic, leukocytosis, C-reactive protein and procalcitonin were elevated, ESR was 80 mm/h. Diagnostic workup including autoimmune markers, viral serology, LTBI-IGRA, PCR test for COVID-19, bacterial and fungal blood cultures were inconclusive for the fever etiology. Laboratory test results are shown in Table 1.Chest X-ray and ECG were also unremarkable. Several other examinations were performed such as bonemarrow biopsy, colonoscopy, bronchoscopy, echocardiogram and were also inconclusive. Chest CT showed the same fibronodular lesion and small patchy infiltration as previous. PET-CT Scan was performed and showed several patchy opacities with low-grade uptake in the left upper lung lobe which were suggestive of pneumonia. Discussed the case with Pneumologist that suggested to start a 7-day course of amikacin but there

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were no clinical improvement and fever persisted. We decided to repeat chest CT and this time there was a new finding of an aneurysm formation and thrombosis in the left upper lobe pulmonary artery segmental branch, thrombosis of the right lower lobe pulmonary artery segmental branches. The venous Doppler ultrasound was negative for lower limbs thrombophlebitis or thrombosis. Pathergy test was performed that was negative. By excluding Behçet disease he was then diagnosed Hughes-Stovin syndrome. He received methylprednisolone pulse followed by oral prednisolone 60 mg/day (1 mg/kg/day), associated with intravenous cyclophosphamide monthly according to 2018 update of the EULAR recommendations for the management of Behçet's disease[7]. Immediately after starting steroids his fever subsided and his clinical condition improved. He was discharged with oral prednisolone and with an indication for hospital admission once monthly for the administration of cyclophosphamide IV which was well tolerated and without any adverse effects. He completed 6 months of the aforementioned plan with gradually tapering down of prednisolone. The control pulmonary angiogram CT showed that the aneurysm in the left upper pulmonary segmental branch remained stable, reduction of thrombosis on the right lower lung segmental branches and the patchy infiltration subsided. At that time, patient refused to continue treatment. One month after stopping the medication he presented with massive hemoptysis and was carried to our ER. He suffered from cardiac arrest and was ressuscitated successfully and transferred to ICU. Chest CT showed left upper lobe pulmonary artery aneurysm rupture with hemorrhage and embolization of left upper pulmonary artery was done by interventional radiologist. However, his clinical condition gradually deteriorated, complicated by severe bilateral pneumonia and was certified dead a few days later.

*Table 1:* Laboratory Data

| Variable | Reference Range, This Hospital | On 3rd Admission | After amikacin treatment | 6th months of diagnosis |
|---|---|---|---|---|
| Hemoglobin (g/dL) | 13.5 - 17.0 | 8.0 | 8.3 | 12.3 |
| HCT (%) | 41 - 53 | 25.5 | 25.8 | 38.0 |
| Mean corpuscular volume (fl) | 80 - 100% | 66.2 | 65.3 | 69.9 |
| White-cell count (x $10^9$/L) | 4.3 - 10 | 15.3 | 26.1 | 8.9 |
| Differential count (x $10^9$/L) | | | | |
| Neutrophils (x $10^9$/L) | 1.9 - 7.3 | 12.9 | 22.7 | 6.3 |
| Eosinophils (x $10^9$/L) | 0.0 - 0.7 | 0.0 | 0.0 | 0.1 |
| Basophils (x $10^9$/L) | 0.0 - 2.0 | 0.1 | 0.0 | 0.1 |
| Lymphocytes (x $10^9$/L) | 1.5 - 4.0 | 1.3 | 2.4 | 1.6 |
| Monocytes (x $10^9$/L) | 0.2 - 0.9 | 1.0 | 1.0 | 0.8 |
| Platelets (x $10^9$/L) | 100 - 400 | 273 | 304 | 171 |
| C-Reactive protein (mg/dL) | <0.5 | 14.98 | 16.98 | 0.12 |
| Procalcitonin (ng/mL) | <0.06 | 10.08 | 0.24 | - |
| Erythrocyte sedimentation rate (mm/hr) | 1.0 - 15.0 | 80.0 | - | 7 |
| CEA (ng/mL) | <3.8 | 1.3 | - | - |
| AFP (ng/mL) | <7.9 | 2.27 | - | - |
| CA 125 (U/mL) | <35 | 6.9 | - | - |
| CA 19.9 (U/mL) | <27 | 9.0 | - | - |
| SCC (ng/mL) | < 1.5 | 0.30 | - | - |
| Transferrin (mg/dL) | 174.0 - 364.0 | 117.0 | - | - |



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| Variable | Reference Range, This Hospital | On 3rd Admission | After amikacin treatment | 6th months of diagnosis |
|---|---|---|---|---|
| Ferritin (ng/mL) | <30-400 | 353.0 | - | - |
| Vitamin B12 (pg/ml) | 197.0 - 771.0 | 373 | - | - |
| Folate (ng/ml) | 3.9 - 26.8 | 7.5 | - | - |
| ANCA | Negative | Negative | - | - |
| Anti-CCP (RU/mL) | <= 5 | 1.52 | - | - |
| Anti-Cardiolipin | Negative | Negative | - | - |
| Immunoglobin A (g/L) | 0.63 - 4.48 | 2.53 | - | - |
| Immunoglobin G (g/L) | 5.40 - 18.22 | 12.94 | - | - |
| Immunoglobin M (g/L) | 0.22 - 2.40 | 0.92 | - | - |
| C3 (g/L) | 0.82 - 1.85 | 1.14 | - | - |
| C4 (g/L) | 0.15 - 0.53 | 0.24 | - | - |
| ANA-Screen | Negative | Negative | - | - |
| COVID-19, PCR assay | Negative | Negative | - | - |
| Cytomegalovirus | | | | |
| IgM | Negative | Negative | - | - |
| IgG | Negative | Positive, 134 U/mL | - | - |
| Epstein-Barr virus | | | | |
| EA-IgG | Negative | Positive, 1:10 | - | - |
| VCA-IgM | Negative | Negative | - | - |
| VCA-IgG | Negative | Negative | - | - |
| EA+EBNA-IgA | Negative | Negative | - | - |
| Interferon gamma release assay | Negative | Negative | - | - |
| Bacterial blood culture | Negative | Negative | - | - |
| Fungal blood culture | Negative | Negative | | |

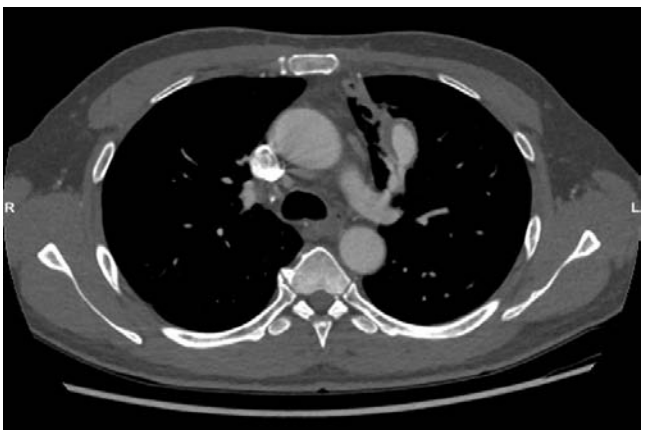

*Figure 2:* Pulmonary artery aneurysm in the segmental branch of left upper pulmonary artery after 6 months of cyclophosphamide and prednisolone. (White arrow)



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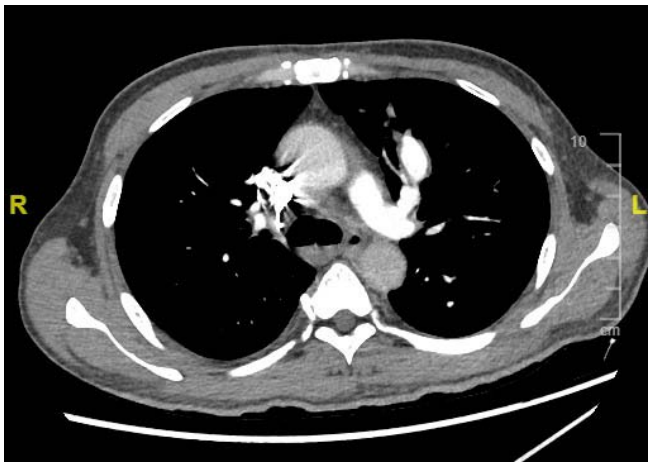


*Figure 1:* Pulmonary artery aneurysm in the segmental branch of left upper pulmonary artery at diagnosis. (White arrow)

## III. Discussion

We presented a challenging case of a 56 years old man with a fever of unknown origin. Initially all the diagnostic work up did not lead to any clue for the etiology of his condition. Even after several courses of antibiotics, some of them of large spectrum, his fever persisted.

Hughes–Stovin syndrome (HSS) is very rare disorder There is no much publication about this disease. Therefore, there is a lack of diagnostic criteria for Hughes-Stovin syndrome. The symptoms of Hughes-Stovin syndrome included hemoptysis (93.0%), cough (94.7%), dyspnea (86.0%), fever (70.2%), weight loss (47.4%), mouth ulcers (19.3%), genital ulcers (10.5%) and pleuritic chest pain (8.8%). [2]The diagnosis of Hughes-Stovin syndrome is based on the finding of pulmonary aneurysm in CT angiography and the findings of deep vein thrombosis in Doppler ultrasound. [3] In our case, the patient only manifested high-grade fever and did not have systemic involvement. His only manifestation was pulmonary artery vasculitis with aneurysm formation. Therefore, it was an unusual type of Hughes-Stovin syndrome.

Hughes-Stovin syndrome has been variably described as "the cardiovascular manifestation of Behcet's disease"[4], "incomplete Behçet's" [5] and "a rare case of Behçet's disease" [6] in literature. Since Hughes-Stovin syndrome is rare disease, there is not a clinical treatment guideline in current literature. Because of similarities of pulmonary involvement between Behçet's disease and Hughes-Stovin syndrome, the treatment guideline for Behçet's disease can used to treat Hughes-Stovin syndrome in current medical practice. [7]

The prognosis of Hughes-Stovin syndrome is poor and aneurysm rupture is the leading cause of death, particularly in aneurysms of arterial origin.

## IV. Conclusion

Hughes–Stovin syndrome (HSS) is very rare disorder characterized by the combination of multiple pulmonary artery aneurysms and deep vein thrombosis. There is no diagnostic criteria and management in current literature due to its rare condition.

We present this case to increase awareness for this condition that unfortunately can lead to death if left undiagnosed and untreated.

## References Références Referencias

1. Khalid and Saleem: Hughes-Stovin Syndrome. Orphanet Journal of Rare Diseases 2011 6:15.
2. Emad Y, Ragab Y, Kechida M, et al. A critical analysis of 57 cases of Hughes-Stovin syndrome (HSS). A report by the HSS International Study Group (HSSISG). *Int J Cardiol*. 2021; 331: 221-229.
3. Al-Jahdali, Massive hemoptysis and deep venous thrombosis presenting in a woman with Hughes-Stovin syndrome: a case report *Journal of Medical Case Reports* 2010, 4: 109
4. Chalazonitis AN, Lachanis SB, Mitseas P, Argyriou P, Tzovara J, Porfyrides P, Sotiropoulou E, Ptohis N. Hughes-Stovin syndrome: a case report and review of the literature. Cases J. 2009 Jan 29; 2: 98.
5. Emad Y, Ragab Y, Shawki Ael H, Gheita T, El-Marakbi A, Salama MH: Hughes-Stovin syndrome: is it incomplete Behcet's? Report of two cases and review of the literature. Clin Rheumatol 2007, 26: 1993-6.
6. Nishi K, Myou S, Ooka T, Taitou H, Fujimura M, Matsuda T: A case of Behcet's disease presenting with Hughes-Stovin syndrome. Nihon Kyobu Shikkan Gakkai Zasshi 1993, 31: 379-384.
7. Hatemi G, Christensen R, Bang D, Bodaghi B, Celik AF, Fortune F, Gaudric J, Gul A, Kötter I, Leccese P,



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Mahr A, Moots R, Ozguler Y, Richter J, Saadoun D, Salvarani C, Scuderi F, Sfikakis PP, Siva A, Stanford M, Tugal-Tutkun I, West R, Yurdakul S, Olivieri I, Yazici H. 2018 update of the EULAR recommend-dations for the management of Behçet's syndrome. Ann Rheum Dis. 2018 Jun;77(6): 808-818.



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# Prevalence of Diabetes Mellitus in the School: A Systematic Review of African Studies

By Agofure Otovwe, Okandeji-Barry Oghenenioborue Rume, Odjimogho Stella & Efegbere Henry

*Abstarct- Introduction:* Diabetes Mellitus (DM) is a metabolic disorder which results in increased glucose level in the blood. When poorly managed it results in morbidity, mortality and low quality of life among patients. The rising prevalence of DM among teachers and students in Africa is becoming disturbing. The authors systematically reviewed studies reporting the prevalence of DM among teachers and students in Africa.

*Materials and Methods:* We searched Pubmed, Google Scholar, Medline, Scopus, African Journal Online, Science Direct, and the Cochrane Library. Using MeSH headings, such as ‘‘diabetes mellitus,’’ ‘‘prevalence,’’ “primary,” “secondary” students,” “teachers,” “educator,” “instructor,” and ‘‘Africa’’ from year 1990 to 2019. Studies included in the systematic review were those that were conducted in primary and secondary schools and utilized the fasting blood sugar (FBS), and the random blood sugar (RBS) test.

*Keywords: diabetes mellitus, prevalence, school, primary, secondary, Africa.*

*GJMR-F Classification: NLMC Code: WG 200.5 G6*


*Strictly as per the compliance and regulations of:*

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# Prevalence of Diabetes Mellitus in the School: A Systematic Review of African Studies

Agofure Otovwe [α], Okandeji-Barry Oghenenioborue Rume [σ], Odjimogho Stella [ρ] & Efegbere Henry [ω]

*Abstract- Introduction:* Diabetes Mellitus (DM) is a metabolic disorder which results in increased glucose level in the blood. When poorly managed it results in morbidity, mortality and low quality of life among patients. The rising prevalence of DM among teachers and students in Africa is becoming disturbing. The authors systematically reviewed studies reporting the prevalence of DM among teachers and students in Africa.

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*Results:* Out of the 12 eligible studies, 6 were conducted among teachers while 6 were conducted among students. The mean age of the students was 14.82±1.84 years while the mean age of the teachers was 43.5±2.59 years. Most of the studies adopted the WHO/IDF diagnostic criteria and the ADA diagnostic criteria. The highest prevalence of DM among teachers was 13.5% while the highest prevalence of DM and prediabetes among students was 1.8% and 28.70% respectively.

*Conclusion:* The review has provided an overview of the prevalence of DM in the school environment in African countries. Consequently, it is hoped it would stimulate 1) more research activities of DM in the school environment 2) implementation of school based policies to mitigate the short and long term impact of DM 3) organization of school based diabetes prevention and management programmes within the school environment.

*Keywords: diabetes mellitus, prevalence, school, primary, secondary, Africa.*

## I. Introduction

The increasing prevalence of diabetes mellitus (DM) has assumed a pandemic proportion worldwide. Middle and lower income countries in sub-Saharan Africa are also experiencing a geometric increase of the disease. According to the International Diabetes Federation an estimated 15.5 million adults aged 20-79 years have diabetes in Africa. The number is expected to increase to 162.5% in year 2045. The estimated number of adolescents and children with type-1 DM in year 2017 was 50,200 in Africa showing the possible escalation of the disease in all age groups [1]. Some of the countries with the highest number of diabetes include Ethiopia with 2.6 million, South Africa with 1.8 million, Democratic Republic of Congo with 1.7 million and Nigeria with 1.7 million people [1]. Furthermore, DM results in micro vascular and macro vascular complications which confers enormous financial burden to families, health system and governments in the continent. This observed burden is related to health system costs incurred by the family and the society in managing the disease, indirect costs resulting from productivity losses due to patient disability and premature mortality, time spent by family members accompanying patients when seeking care, and intangible costs (psychological pain to the family and loved ones) [2].

Various population based studies have reported the prevalence of diabetes in Africa [3,4,5,6,7, 8,9]. A component of the entire population in Africa where diabetes seems to be on the increase is the school environment. The prevalence of DM on the school would be devastating both to teachers and students. For teachers living with DM would be very challenging in performing their daily duties especially as it relates to caring for children under their care. This is because students spend between 6-8 hours every day in school, thus conferring a lot of responsibility on the teachers. For students living with DM would struggle to adapt to the required personal and environmental changes required to manage the condition. This is because at this age they are carefree and are usually involve in a lot of activities such as physical activities, dietary habits such as eating sweets, taking soft drinks and snacks which could be inimical to their health as they could be committed to lifelong monitoring and regulating blood sugar levels through insulin therapy and other relevant

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medications [10]. School teachers belong to the group of literate working class and contribute to the level of awareness of the larger society on many issues. However, there is paucity of studies in Africa that have systematically reviewed and documented the prevalence of DM among teachers and students; hence, the focus of this review.

*a) Objectives*

- To highlight the prevalence of DM among teachers and students
- To underline the diagnostic criteria used in diagnosing

## II. Materials and Methods

*a) Study design*

This is a systematic review of the prevalence of DM among teachers and students in both primary and secondary schools in Africa countries following the MOOSE guidelines for systematic reviews and observational studies [11]. The included studies were extracted by two of the authors AO and OOR using standardized data extraction forms. Characteristics of identified studies extracted were the study location, year of study, study design, sample size, diabetes mellitus diagnostic criteria, age, and prevalence of DM.

*b) Study area*

The study area comprised all regions of Africa including South, East, West, North and Central Africa.

*c) Data sources and searches*

A systematic collation of published data over the period of year 1990 to 2019 on prevalence of DM among teachers and students was retrieved between May and October 2019 to develop an all-inclusive distribution of DM in both primary and secondary schools in Africa. The authors searched electronic online bibliographic archives such as Pubmed, Google Scholar, Medline, Scopus, African Journal Online, Science Direct, and the Cochrane Library. Using MeSH headings, the terms ''diabetes mellitus,'' ''prevalence,'' "primary," secondary," "students" "teachers," "educator," "instructor," and ''Africa'' as well as variations thereof were searched for. We contacted the authors of articles in journals that were not available online. The last search was performed on 12 October, 2019. Studies included in the systematic review were those that were conducted in primary and secondary schools and utilized the fasting blood sugar (FBS), the random blood sugar (RBS) test. In all, a total of 12 studies involving 6360 teachers and students were evaluated. Thus, 6 studies comprising 2191 teachers and 6 studies comprising 4169 pupils and students were included in the systematic review.

*d) Inclusion Criteria*

Only school-based studies among teachers and students that were executed between 1990 and 2019 in Africa and in which FBS, RBS or self report through questionnaire was used to diagnose DM were included in the systematic review. Furthermore, included studies were prospective or cross sectional studies published in English language.

*e) Exclusion Criteria*

Excluded studies from the systematic review were those carried out before 1990, in the university and other tertiary schools, those published in other languages aside English, those carried out among other staffs of primary and secondary schools aside teachers and those without clear definition of how DM was diagnosed.

*f) Ethical Consideration*

This review was the preliminary phase of a larger study among teachers, students and community participants of which ethical approval was obtained from the Delta State Ethical Review Committee.

*g) Study selection and Data Extraction*

For teachers a total of 2408 potential articles were indicated in the initial literature search after removing duplicates, of which 22 full text articles were screened for eligibility and only 6 studies were included in the qualitative synthesis (Fig 1). For students 5538 potential articles were indicated in the initial literature search after removing duplicates, of which 31 full text articles were screened for eligibility and only 6 studies were included in the qualitative synthesis (Fig 2). Various data were extracted from eligible studies, such as the prevalence of DM, method of diagnosing DM, study design, sample size and African country in which the study was carried out. A summary of the data extracted is as shown in Table 1. We coded the data based on the name of the first author of the study and the year that the study was published.

*h) Quality of the Studies Included*

Two authors AO and OOR separately assessed the quality of the studies included using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [12]. The studies were assessed with questions appropriate to the study design. We graded the quality of the study as good (G) if its rating was at least 70%, fair (F) if it's rating was at least 50%, and poor (P) if it's rating was less than 50% [3].

*i) Data analysis*

All the relevant information was entered into an Excel spreadsheet and data analysis was performed using SPSS (Version 20 for Windows, SPSS Inc., Chicago, IL).

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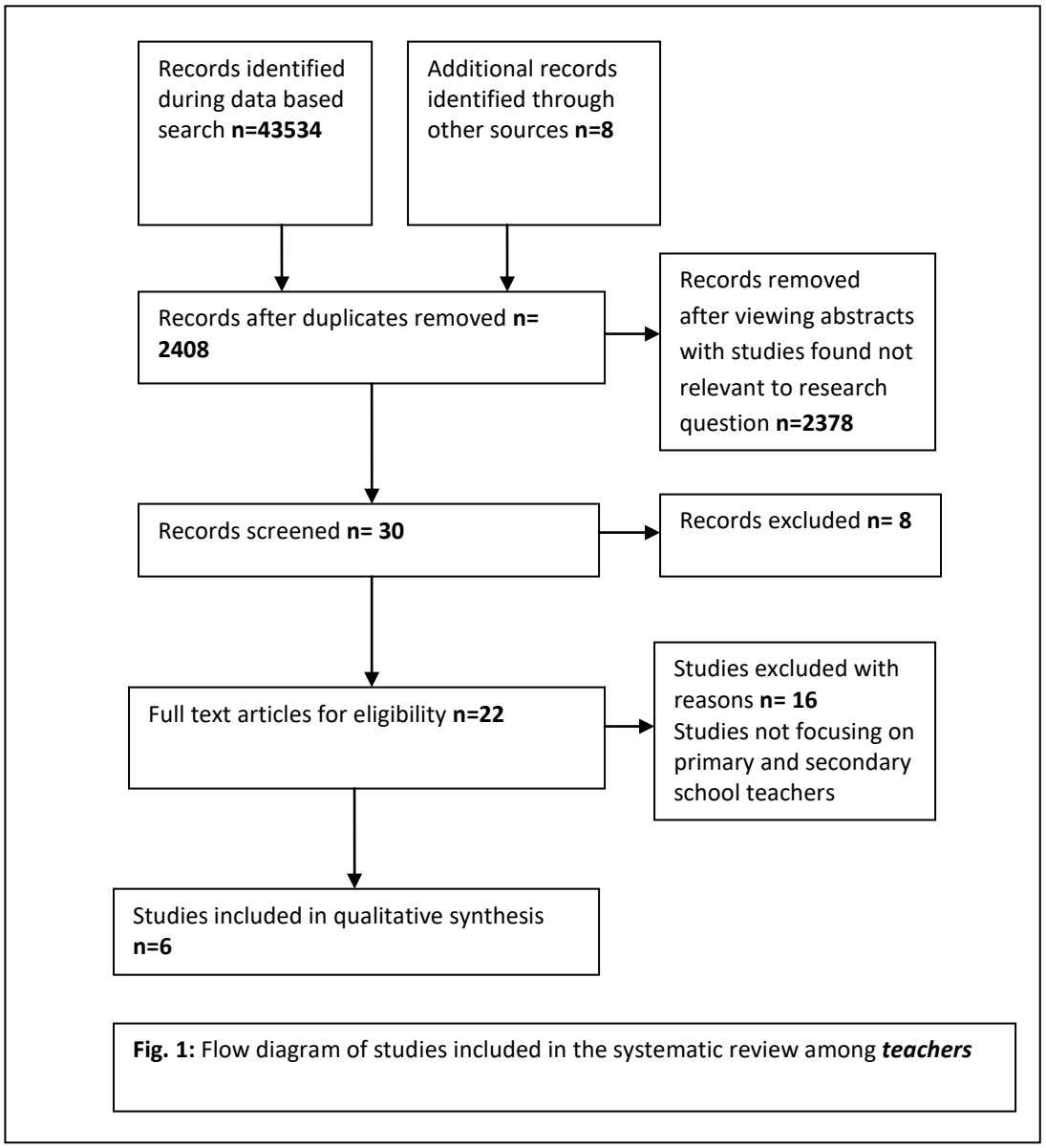


*Fig. 1:* Flow diagram of studies included in the systematic review among *teachers*



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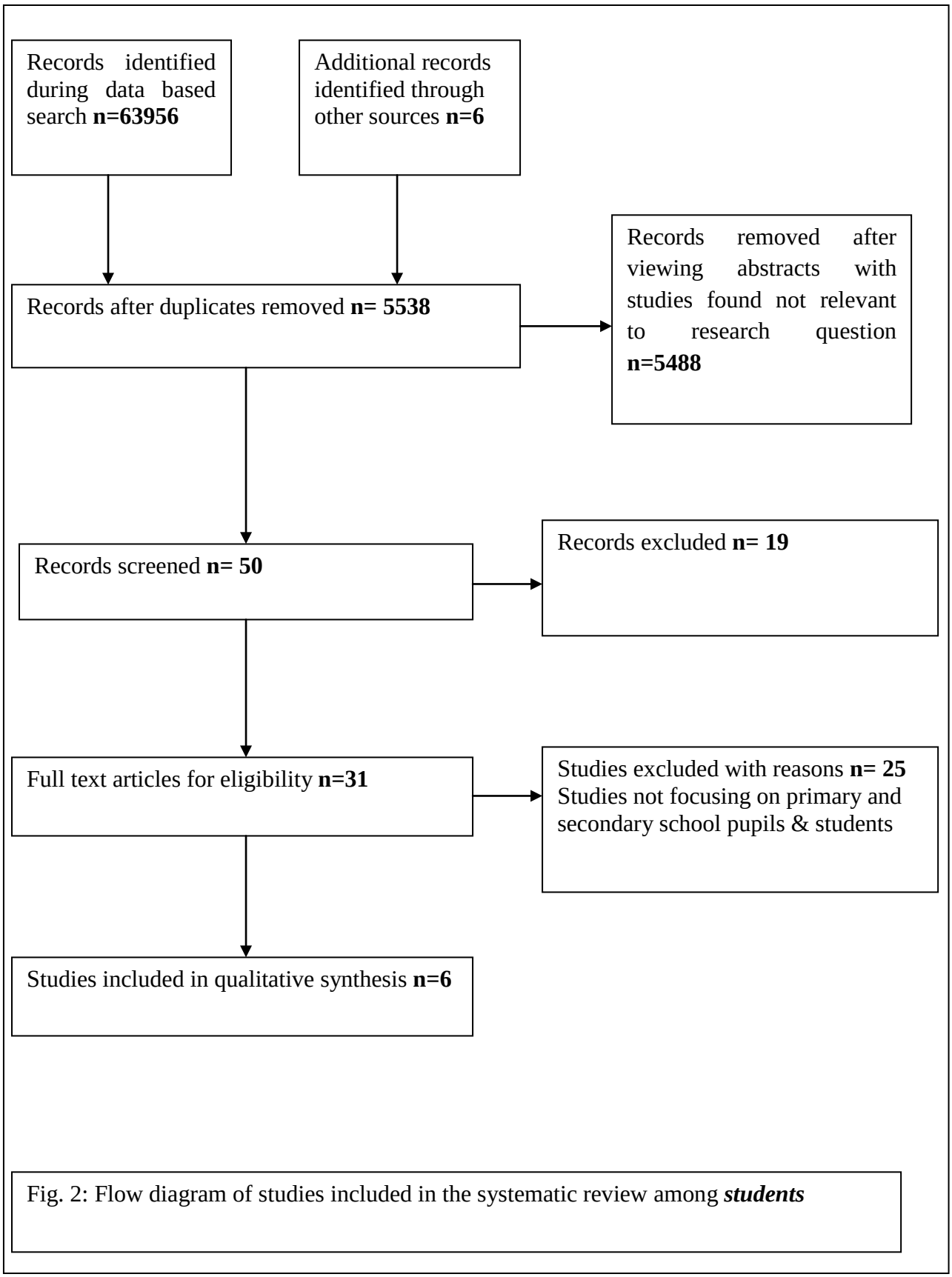


*Fig. 2:* Flow diagram of studies included in the systematic review among *students*



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## III. Results

*a) Study characteristics*

All of the 6 eligible studies among teachers were carried out from year 2015-2017 and were school based cross sectional studies. The highest population of 517 teachers was associated with the study in South Africa [13], while the least population was a study in Nigeria among 83 teachers [14]. The ages of the teachers in the studies [13,14,15,16,17,18] ranged from 40-46 years with a mean age of 43.5±2.59 years. Only two studies reported mean glucose; one reported a mean glucose of 5.1±0.9 mmol/l [14] and the other reported a mean glucose of 4.65±2.3 mmol/l [13]. In addition, 50% of the studies were conducted in Secondary Schools and 33.3% in Primary schools. The highest prevalence of DM as reported by the study in South Africa [16] was 13.50%, while the least reported prevalence was 1.2% [14]. The diagnostic criteria adopted by the studies among teachers [13,14,15,16,18] were World Health Organisation and International Diabetes Federation harmonized definition of Diabetes mellitus and only one of the study adopted the International Diabetes Federation diagnostic criteria [17]. In addition, 50% of the study adopted the FBS for their diagnosis [16,17,18] while the other 50% adopted the RBS [13,14,15] (Table 1).

All of the 6 eligible studies among students were carried out from year 2006-2019 and were school based cohort [19] and cross sectional studies [20,21,22,23,24]. The highest population of 880 students was associated with the study in Nigeria [21]. The ages of the students in the studies ranged from 10-19 years with a mean age of 14.82±1.84 years. Four studies reported mean glucose with the highest mean glucose of 4.8±0.5 mmol/l [19,20,21,22]. All studies were conducted in Secondary Schools. The highest prevalence of prediabetes as reported by the study in Nigeria [23] was 28.70%, while the least reported prevalence was 6.4% [24]. In addition, the highest prevalence of DM was 1.8% [19] (Table 2).

*Table 1:* Demographic and Clinical Characteristics of Studies included in the systematic review among teachers

| Country | Year | Study Design | Sample Size | Mean Age | Mean Glucose | Types of schools | Prevalence of DM (%) | Diagnostic Criteria | | Reference | Quality |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | WHO/IDF | IDF | | |
| South Africa | 2016 | Cross sectional | 489 | 46.3 years | - | Secondary | 10.1% | RBS≥11.1 mmol/l | | Laurence et al. [15] | Good |
| Nigeria | 2017 | Cross-sectional | 118 | 43 years | - | Secondary | 2.8% | | FBS≥7.0mmol/l or 126mg/dl | Ilesanmi et al. [17] | Fair |
| Tanzania | 2016 | Cross sectional | 229 | 40 years | - | Primary | 8.3% | FBS≥7.0mmol/l or 126mg/dl | | Chiwanga et al. [18] | Good |
| Nigeria | 2016 | Cross sectional | 83 | 46 years | 5.1±0.9 mmol/l | Secondary | 1.2% | RBS≥11.1 mmol/l | | Akintunde & Oloyede [14] | Fair |
| South Africa | 2015 | Cross sectional | 455 | - | - | Primary, Secondary,Intermediate | 13.5% | FBS≥7.0mmol/l | | Dalal et al. [16] | Fair |
| South Africa | 2015 | Cross sectional | 517 | 45±7.9 years | 4.65±2.3 mmol/l | Primary | 2.0% | RBS≥200mg/dl | | Senekal et al. [13] | Good |

*Table 2:* Demographic and Clinical Characteristics of Studies included in the systematic review among Students

| Country | Year | Study Design | Sample Size | Mean Age | Mean Glucose | Types of schools | Prevalence of Prediabetes (%) | Prevalence of DM (%) | Reference | Quality |
|---|---|---|---|---|---|---|---|---|---|---|
| Cameroon | 2019 | Cohort | 815 | 18 years | 0.89±0.34 g/l | Secondary | - | 1.8% | Kandema et al. [19] | Good |
| South Africa | 2006 | Cross-sectional | 338 | 12.7±1.9 years | 4.26±0.63 mmol/l | Secondary | - | 0.0% | Somers et al. [20] | Fair |
| Nigeria | 2019 | Cross sectional | 880 | 15.01±2.1 years | - | Secondary | 17.3% | - | Jaja & Yarhere, [21] | Good |
| Nigeria | 2012 | Cross sectional | 820 | 13.6±2.2 years | - | Secondary | - | 0.3% | Okpere et al. [22] | Fair |
| Uganda | 2018 | Cross sectional | 688 | 15.4±1.7 years | 4.8±0.5 mmol/l | Secondary | 6.4% | - | Nakiriba et al. [23] | Fair |
| Nigeria | 2015 | Cross sectional | 628 | 14.2±1.7 years | 95.3±10.9 mg/dl | Secondary | 28.70% | 0.6% | Oluwayemi et al. [24] | Good |

*Okpere et al., was diagnosed through self report*



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Two of the selected studies [19,23] adopted the American Diabetes Association definition of DM. Another study adopted WHO [24] and the Expert Committee on the Diagnosis and Classification of DM [20]. Another study adopted the International Society for Paediatrics and Adolescent Diabetes guidelines for classification of diabetes mellitus [21] (Table 3).

*Table 3:* Diagnostic criteria adopted by the selected studies among students

| | ADA | ECDCDM | ISPAD | WHO |
|---|---|---|---|---|
| Oluwayemi et al. [23] | FBG≥126mg/dl | | | |
| Kandema et al. [19] | FBS≥126mg/dl | | | |
| Somers et al. [20] | | FBS≥7.0mmol/l | | |
| Jaja & Yarhere [21] | | | FBS≥7.0mmol/l or 126mg/dl | |
| Nakiriba et al. [24] | | | | FBS≥7.0mmol/l or 126mg/dl |

*Okpere et al., 2012 was not reflected because blood glucose test was not carried out due to lack of permission from school authorities*

*FBS-Fasting blood Sugar, RBS-Random Blood Sugar, WHO-World Health Organisation, IDF-International Diabetes Federation, ADA-American Diabetes Association, ECDCDM-Expert Committee on the Diagnosis & Classification of diabetes mellitus, ISPAD-International Society for Paediatrics and Adolescent Diabetes guidelines for classification of diabetes mellitus*

The prevalence of DM among the teachers was as high as 13.5% [16] with the least as 1.2% [14] (Fig. 3). For the students, prevalence of DM was 1.8% [19] and least was 0.0% [20]. However, three studies reported the prevalence of prediabetes to be 28.70% [23], 17.30% [21] and 6.40% [24] (Fig 3).

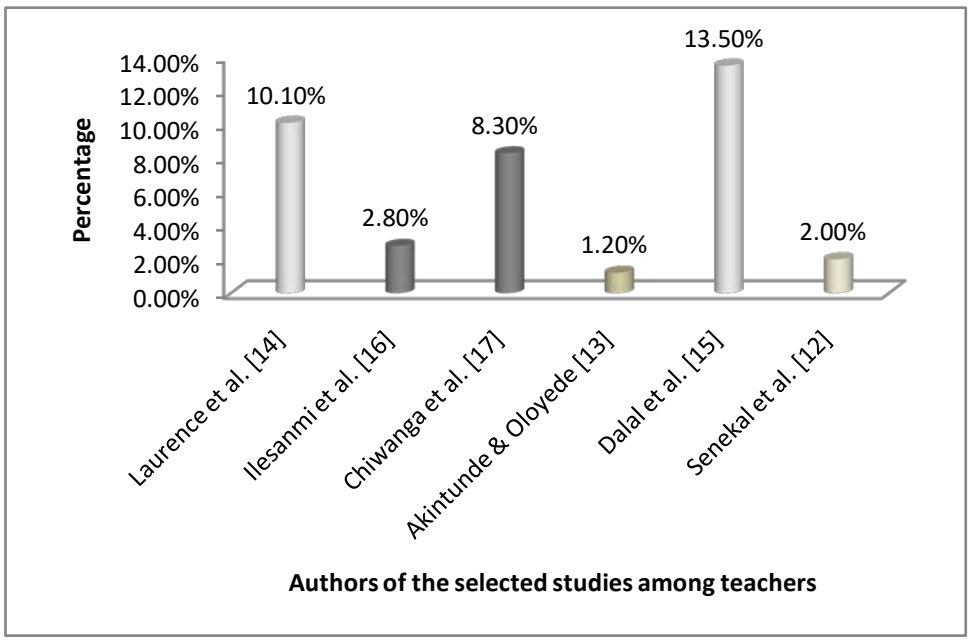


*Figure 3:* Prevalence of diabetes mellitus among the teachers



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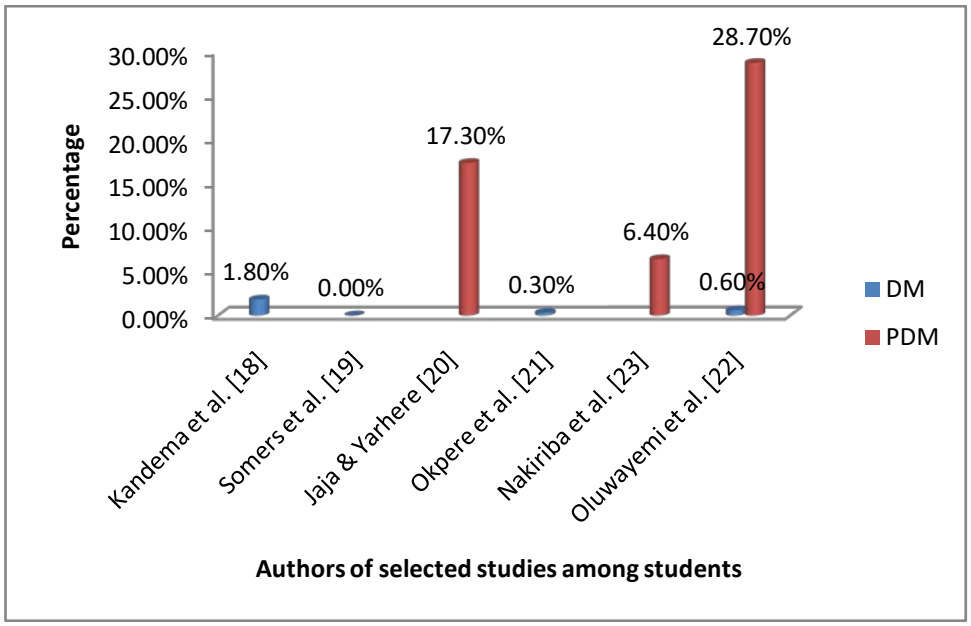


*Figure 4:* Prevalence of diabetes mellitus and pre-diabetes mellitus
*Key: DM-Diabetes mellitus, PDM-Pre-diabetes mellitus*

## IV. Discussion

This systematic review highlighted the prevalence of DM among teachers and students in schools to stimulate necessary actions in preventing the disease and reducing diabetes related complications in the school. This review became necessary as most previous review on DM focused on patients diagnosed in clinical settings and the general population [3,25,26,27,28]. The prevalence of DM among the teachers was 13.50% [16], 10.10% [15], and 8.3% [18]. This observed prevalence of DM among the teachers is in line with the trend of DM among adults in Africa. Type-2 DM is the most prevalent form of diabetes in Africa and these findings corroborates other community and population based findings on prevalence of DM in Africa [3,4,5,6,7,8,9]. The clinical significance of the findings is that just as the healthcare system and the general population is currently contending with the increasing rate of DM and its complications; teachers could also be contending with the morbidity associated with DM including its effect on individual, family and work. This may possibly be devastating to the school as teachers would not have to only focus on the pupils and students under their care; but would have to spend time even within school hours to manage DM. This could result in emotional and mental stress, loss of manpower and low productivity. The prevalence of DM among teachers is peculiar because teachers are change agent in impacting knowledge not only within the school environment but also in the community especially in developing countries of Africa.

The prevalence of prediabetes recorded among students in the selected studies suggests a likely escalation of type-1 DM among students in Africa in the not too distant future. This is because for countries like Nigeria with a high population of adolescents and youths making up about 62.15% of the general population [29]; thus an escalation of DM would be devastating to families, healthcare system and the nation. The highest recorded prevalence of type-1 DM of 1.8% or 18 per 1000 in the review was higher than that obtained in studies of over twenty years ago in Nigeria 0.33 per 1000 and 0.95 per 1000 among Sudanese children [30,31]. This increasing prevalence suggests the possible escalation of DM among this population in Africa which has been forecasted [1]. The clinical significance and implication is that African schools like their American and European counterpart would be dealing with children with type-1 DM in the school. This is coupled with the current prevalence of type-2 DM among teachers. Thus, the issue of DM in the school environment should be given the desired attention through creating awareness programmes among staffs and students including training and retraining of teachers on how to handle a DM situation in the school.

In diagnosing diabetes, various diagnostic guidelines have been developed and updated over the years [32,33,34,35]. However, despite the evolvement, improvement and recommendation by various organizations concerned with DM diagnosis various studies still adopt the diagnostic criteria that are convenient for their study. In the review among teachers studies that adopted the WHO/IDF definition of DM reported prevalence of DM to be 10.1% [16], 1.2% [15], 8.3% [19], 13.5% [16], and 2.0% [13] while the sole study that adopted the IDF criteria reported a prevalence of 2.80% [17] Table 1.



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The studies carried out among students showed more variation in their diagnostic criteria. Two studies used ADA definition and they reported prevalence of prediabetes of 28.70% and DM 0.6% [23] and 1.8% [19]. Furthermore, one study used the Expert Committee on the Diagnosis and Classification of DM and it reported a prevalence of 0% [20]. Similarly, one of the studies utilized the International Society for Paediatrics and Adolescents Diabetes guidelines reported the prevalence of prediabetes to be 17.3% [21] and the study that adopted the WHO guidelines reported a prevalence of prediabetes to be 6.4% [24] Table 2.

The prevalence of prediabetes and DM among students and teachers has brought to the forefront the issue of DM in the school and the need for implementing prevention and management programmes in both primary and secondary schools so as to stem the tide of DM among this cohorts.

*Limitation of the study*

The review was a retrospective study of previous published studies. Therefore, the authors relied solely on the report of the selected studies in writing the review.

## V. Conclusion

The systematic review highlighted the prevalence of DM in teachers and students both in primary and secondary schools in Africa. Therefore, it is pertinent for stakeholders in the education ministry in collaboration with the health ministry to implement prevention programmes such as screening and creation of awareness of DM in the school environment. This would help in achieving health promoting schools which is a prerequisite for achieving the Sustainable Goal 3.

*Contributions*

*OA:* Contributed to the concept, design, data searches and extraction, analysis, manuscript preparation and writing

*OOR:* Contributed to the design, data searches and extraction, analysis, manuscript preparation and review

*OS:* Contributed to the design, analysis, manuscript preparation and review

*EH:* Contributed to the design, analysis, manuscript preparation and review

## References Références Referencias


1. International Diabetes Federation 2017. Diabetes Atlas 8th Edition. http://www.diabetesatlas.org.
2. Kirigia JM, Sambo HB, Sambo LG, Barry SP. Economic burden of diabetes mellitus in the WHO African region. BMC International Health and Human Rights 2009; 9(6).
3. Uloko AE, Musa BM, Ramalan MA, Gezawa ID, Puepet FH, Uloko AT., et al. Prevalence and Risk Factors for Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. Diabetes Therapy 2018; 9(3): 1307-1316.doi: 10.1007/s13300-018-0441-1.
4. Olatunbosun ST, Ojo PO, Fineberg NS, Bella AF. Prevalence of diabetes mellitus and impaired glucose tolerance in a group of urban adults in Nigeria. J Natl Med Assoc 1998; 90:293-301.
5. Bradshaw D, Norman R, Pieterse D, et al. Estimating the burden of disease attributable to diabetes in South Africa in 2000. South Afr Med J 2007; 97:700–6.
6. Bertram MY, Jaswal AV, Van Wyk VP, et al. The non-fatal disease burden caused by type 2 diabetes in South Africa, 2009. Glob Health Action 2013; 6:19244. doi:10.3402/gha.v6i0.19244
7. Oti SO, van de Vijver S, Agyemang C, Kyobutungi C. The magnitude of diabetes and its association with obesity in the slums of Nairobi, Kenya: results from a cross-sectional survey. Tropical Med Int Health 2013; 18(12): 1520–30.
8. Ayah R, Joshi MD, Wanjiru R, Njau EK, Otieno CF, Njeru EK, et al. A population-based survey of prevalence of diabetes and correlates in an urban slum community in Nairobi, Kenya. BMC Public Health 2013; 13(1):371.
9. Christensen DL, Friis H, Mwaniki DL, Kilonzo B, Tetens I, Boit MK, et al. Prevalence of glucose intolerance and associated risk factors in rural and urban populations of different ethnic groups in Kenya. Diabetes Res Clin Pract. 2009; 84(3):303–10.
10. Aljehany B. The impacts of a health education programme on primary school teachers' knowledge and attitudes towards type 1 diabetes mellitus in children in Saudi Arabia. A thesis submitted in fulfillment of the requirements for the degree of doctor of philosophy at the University of Salford Manchester 2016.
11. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283:2008–20012.
12. National Heart Lung and Blood Institute. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Available from: https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/coh ort. Accessed 28 May 2017.
13. Senekal M, Seme Z, de Villiers A, Steyn NP. Health status of primary school educators in low socio-economic areas in South Africa. BMC Public Health 2015; 15(186).




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14. Akintunde AA, Oloyede TW. Metabolic syndrome and occupation: Any association? Prevalence among auto technicians and school teachers in South West Nigeria. Diabetes Metab Syndr 2017; 11 Suppl 1:S223-S227.
15. Laurence EC, Volmink J, Esterhuizen TM, Dalal S, Holmes MD. Risk of cardiovascular disease among teachers in Cape Town: Findings of the South African PaCT pilot study. SAMJ 2016; 106(10).
16. Dalal S, Holmes MD, Laurence C, Bajunirwe F, Guwatudde D, Njelekela M, et al. Feasibility of a large cohort study in sub-Saharan Africa assessed through a four-country study, Global Health Action 2015; 8:1, 27422, DOI: 10.3402/gha.v8.27422.
17. Ilesanmi OS, Ojo OA, Omotoso B, Ojo OE, Junaid OA, Amenkhienan I, et al. Prevalence of diabetes mellitus and the associated behavioral risks factors among the staff of three secondary schools in Owo, Ondo State, Nigeria. Research Journal of Health Science 2017; 5(3).
18. Chiwanga FS, Njelekela MA, Diamond MB, Bajunirwe F, Guwatudde D, Nankya-Mutyoba J, et al. Urban and rural prevalence of diabetes and prediabetes and risk factors associated with diabetes in Tanzania and Uganda. Global Health Action 2016; 9:31440.
19. Kamdema F, Lemogoumb D, Jingic AM, Guetchuina SC, Kenmegnea C, Douallaa MS, et al. Prevalence and determinants of abnormal glucose metabolism in urban and rural secondary schools in Cameroon: A cross-sectional study in a sub-Saharan Africa setting, Primary Care Diabetes (2019). https://doi.org/10.1016/j.pcd.2019.02.00.
20. Somers A, Rusford E, Hassan MS, Erasmus RT. Screening for diabetes mellitus in learners residing in the Belhar, Delft and Mfuleni communities of Cape Town, Western Cape, South Africa. SA Fam Pract 2006; 48(6): 16.
21. Jaja T, Yarhere IE. Risk factors for type 2 diabetes mellitus in adolescents secondary school students in Port Harcourt, Nigeria. Nigerian Journal of Paediatrics 2015; 42(2):137-141.
22. Okpere AN, Anochie IC, Eke FU. Prevalence of Microalbuminuria among secondary school children. African Health Sciences 2012; 12(2).
23. Oluwayemi IO, Brink SJ, Oyenusi EE, Oduwole OA, Oluwayemi MA. Fasting Blood Glucose Profile among Secondary School Adolescents in Ado-Ekiti, Nigeria. Journal of Nutrition and Metabolism 2015; Article ID 417859, 4 pages.
24. Nakiriba R, Mayega RW, Piloya T, Nabukeera-Barungi N, Idro R. Prevalence and factors associated with dysglycemia among girls in selected boarding secondary schools in Wakiso District, Uganda. Adolescent Health, Medicine and Therapeutics 2018; 9:167–176.
25. Asmelash D, Asmelash Y. The Burden of Undiagnosed Diabetes Mellitus in Adult African Population: A Systematic Review and Meta-Analysis. Journal of Diabetes Research / 2019, Volume 2019 |Article ID 4134937 | 8 pages.
26. Werfalli M, Musekiwa A, Engel ME, Ross I, Kengne AP, Levitt NS. The prevalence of type 2 diabetes mellitus among older people in Africa: a systematic review study protocol. BMJ Open 2014; 4:e004747.
27. Adeloye D, Ige JO, Aderemi AV, Adeleye N, Amoo EO, Auta A et al. Estimating the prevalence, hospitalisation and mortality from type 2 diabetes mellitus in Nigeria: a systematic review and meta-analysis. BMJ Open 2017; 7:e015424.
28. Chivese T, Werfalli MM, Magodoro I, Chinhoyi RL, Kengne AP, Norris SA et al. Prevalence of type 2 diabetes mellitus in women of childbearing age in Africa during 2000–2016: a systematic review and meta-analysis. BMJ Open 2019; 9(5): e024345.
29. The World Factbook — Central Intelligence Agency". *www.cia.gov*. Retrieved 10 April 2018.
30. Mbanya JC, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetesinsub-Saharan Africa. Lancet 2010; 375(9733): 2254-66.
31. Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. Diabetes Care 2011; 34(6):1249–57.
32. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997; 20:1183–1197.
33. Diabetes mellitus. Report of a WHO Study Group. World Health Organisation Technical Report Service. 1985; 727: 1–113.
34. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003; 26:3160–3167.
35. Gillett MJ. International Expert Committee report on the role of the A1c assay in the diagnosis of diabetes: Diabetes Care 2009; 32(7): 1327-1334. Clin Biochem Rev. 2009; 30:197–200.




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# Neuronal Degeneration: Its Neuropathological and Histopathological Aspects as One of the Causes of the Etiology of Alzheimer's Disease

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*Abstarct-* This article aims to propose neuronal degeneration, and its neuropathological and histopathological aspects, as one of the causes of the etiology of Alzheimer's disease. The research had a qualitative approach and a bibliographic review, based on information from the last 10 years in the Scientific Electronic Library Online (Scielo), Digital Library of Theses and Dissertations (BDTD) and Digital Repository of the University of Beira (Ubibliorum) databases., website in general and consultations by reference theorists. The research concluded that there is a relationship between neuronal degeneration as one of the causes of AD etiology, and its histopathological and neuropathological aspects, such as accumulation of senile plaques composed of Ab-amyloid proteins, phospharization of tau protein, and neurotoxic gases from acetylcholimestarse enzyme.

*Keywords:* *alzheimer's disease. tau protein. senile plaques. acetylcholine.*

*GJMR-F Classification:* *NLMC Code: WT 155*

NEURONALDEGENERATIONITSNEUROPATHOLOGICALANDHISTOPATHOLOGICALASPECTSASONEOFTHECAUSESOFTHEETIOLOGYOFALZHEIMERSDISEASE

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# Neuronal Degeneration: Its Neuropathological and Histopathological Aspects as One of the Causes of the Etiology of Alzheimer's Disease

## Degeneração Neuronal: Seus Aspectos Neuropatológicos E Histopatológicos Como Uma Das Causas Da Etiologia Da Doença De Alzheimer

## Degeneración Neuronal: Sus Aspectos Neuropatológicos E Histopatológicos Como Una De Las Causas De La Etiología De La Enfermedad De Alzheimer

Eraldo Sales [α] & Benedita Nadia Silva Pereira [σ]

*Resumo-* Esse artigo tem o objetivo de propor a degeneração neuronal, e seus aspectos neuropatológicos e histopatológicos, como uma das causas da etiologia da doença de Alzheimer. A pesquisa foi de abordagem qualitativa e de revisão bibliográfica, a partir de informações dos últimos 10 anos nas bases de dados Scientific Electronic Library Online (Scielo), Biblioteca Digital de Teses e Dissertações (BDTD) e Repositório Digital da Universidade da Beira (Ubibliorum), site em geral e consultas de teóricos de referências. A pesquisa concluiu que há relação entre a degeneração neuronal como uma das causas da etiologia da DA, e seus aspectos histopatológicas e neuropatológicas, como acúmulo das placas de senis compostas pelas proteínas Ab-amilóide, da fosfarização da proteína tau, e dos gases neurotóxicos da enzima acetilcolimestarse.

*Palavras-Chave: doença de alzheimer. proteína tau. placas senis. acetilcolina.*

*Abstract-* This article aims to propose neuronal degeneration, and its neuropathological and histopathological aspects, as one of the causes of the etiology of Alzheimer's disease. The research had a qualitative approach and a bibliographic review, based on information from the last 10 years in the Scientific Electronic Library Online (Scielo), Digital Library of Theses and Dissertations (BDTD) and Digital Repository of the University of Beira (Ubibliorum) databases., website in general and consultations by reference theorists. The research concluded that there is a relationship between neuronal degeneration as one of the causes of AD etiology, and its histopathological and neuropathological aspects, such as accumulation of senile plaques composed of Ab-amyloid proteins, phospharization of tau protein, and neurotoxic gases from acetylcholimestarse enzyme.

*Keywords: alzheimer's disease. tau protein. senile plaques. acetylcholine.*

*Resumèn-* Este artículo tiene como objetivo proponer la degeneración neuronal, y sus aspectos neuropatológicos e histopatológicos, como una de las causas de la etiología de la enfermedad de Alzheimer. La investigación utilizó un enfoque cualitativo y una revisión bibliográfica, basada en información de los últimos 10 años en la Biblioteca Científica Electrónica en Línea (Scielo), la Biblioteca Digital de Tesis y Disertaciones (BDTD) y el Repositorio Digital de la Universidad de Beira (Ubibliorum), Web en general y consultas por teóricos de referencia. La investigación concluyó que existe una relación entre la degeneración neuronal como una de las causas de la etiología de la EA y sus aspectos histopatológicos y neuropatológicos, como la acumulación de placas seniles compuestas por proteínas amiloides Ab, la fosforización de la proteína tau y los gases neurotóxicos de la acetilcolimestarse. enzima.

*Palabras-clave: enfermedad de alzheimer. proteína tau. placas seniles. acetilcolina.*

## I. Introdução

Em 1906, o psiquiatra e neuropatologista alemão, Alois Alzheimer, confirmou que sua paciente Auguste Deter, sofria de uma doença estranha no córtex cerebral manifestada por deficiência progressiva de memória e outros problemas cognitivos e comportamentais. Todavia, foi somente com a morte de Auguste Deter, em 1910, quando examinou seu encéfalo, quando pode confirmar que as neufibrilas, elementos do citoesqueleto, causavam acúmulos e formavam feixes e que gradualmente avançavam em direção à superfície celular, causando assim, a morte dos neurônios.

E a partir desta descoberta, e com o avanço do conhecimento sobre a doença, e através de estudos e pesquisas, chegou-se a confirmação de que DA é uma patologia neurodegenerativa mais frequente associada à idade, cujas manifestações cognitivas e neuropsiquiátricas resultam em deficiência progressiva e incapacitação. A doença afeta aproximadamente 10% dos indivíduos com idade superior a 65 anos e 40% acima de 80 anos. O envelhecimento acompanhado pelas síndromes demenciais é uma realidade que tende a aumentar nos próximos anos e em especial na velhice avançada.

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Projeções de prevalência e incidência indicam que ocorrerá um crescimento mais elevado do número de pessoas com demência no mundo. Estima-se que o número total de pessoas que sofrem de demência mundial é de 35,6 milhões e é previsto que este número quase dobre a cada 20 anos – para 65,7 milhões em 2030 e 115,4 milhões em 2050. O número total de novos casos de demência a cada ano, no mundo, é de quase 7,7 milhões, o que implica um novo caso a cada quatro segundos, uma doença que apaga as memórias e afeta cerca de 1,2 milhão de pessoas no Brasil.

Os estudos tem como objetivo geral apontar a degeneração neuronal, e seus aspectos neuropatológicos e histopatológicos, como uma das causas da etiologia da DA. Justificam-se os estudos sobre a referida temática e dar-se-á por ser um tema de bastante relevância tanto para a ciência, quanto para a população como um todo, pois os estudos dos marcadores neuropatológicos e histopatológicos como uma das causas da etiologia da degeneração da DA, representam um grande avanço, pois espera-se que biomarcadores de qualidade, como APP ΔC31, atraiam mais estudos para validação e representem um novo alvo para o diagnóstico e desenvolvimento terapêutico da DA. A pesquisa de cunho bibliográfico nos permitirá um aprofundamento maior da temática, a partir de informações nos últimos 10 anos nas bases de dados plataformas Scientific Electronic Library Online (Scielo), Biblioteca Digital de Teses e Dissertações (BDTD) e Repositório Digital da Universidade da Beira (Ubibliorum), site em geral, e em literaturas de autores pertinentes sobre o assunto.

## II. Metodologia

A pesquisa teve cunho qualitativo com delineamento bibliográfico do tipo Revisão de Literatura Integrativa e descritiva, considerando o objetivo principal de conhecer a degeneração neuronal, e seus aspectos neuropatológicos e histopatológicos, como uma das causas da etiologia da doença Alzheimer, a partir de trabalhos publicados sobre o tema. Esse método possibilita a análise de estudos já realizados, de modo que seja possível, além de uma busca e levantamento da literatura existente sobre uma determinada temática, a análise crítica dos estudos incluídos (SOUZA, SILVA & CARVALHO, 2010). Além disso, a revisão integrativa permite a síntese de conhecimento e a reflexão sobre a aplicabilidade de resultados dos estudos significativos publicados, sendo realizada a partir do cumprimento de algumas etapas, sendo elas: 1. elaboração da pergunta norteadora para o levantamento bibliográfico; 2. elaboração dos critérios de inclusão/exclusão; 3. escolha dos descritores e 4. escolha das bases de dados na prática (SOUZA, SILVA & CARVALHO, 2010). Desse modo, pretende-se, com tal metodologia, estabelecer maiores conhecimentos sobre a degeneração neuronal, e seus aspectos neuropatológicos e histopatológicos, como uma das causas da etiologia da doença Alzheimer, nos casos de Alzheimer o embasamento para práticas clínicas e interventivas concretas por partedos profissionais.

Com intuito de responder à pergunta "Qual é o impacto da degeneração neuronal, e seus aspectos neuropatológicos e histopatológicos, como uma das causas da etiologia da doença Alzheimer?", essa revisão de literatura foi elaborada por meio de registros, organização e análise de dados bibliográficos – aspectos que permitem uma maior compreensão e interpretação crítica sobre o assunto. As plataformas de busca utilizadas foram Scientific Electronic Library Online (Scielo), Biblioteca Digital de Teses e Dissertações (BDTD) e Repositório Digital da Universidade da Beira (Ubibliorum), site em geral, e em literaturas de autores pertinentes sobre o assunto.

Os descritores utilizados foram "degeneração neuronal" *and* "Alzheimer", de acordo com os Descritores em Ciências da Saúde (DeCS). Os critérios de inclusão foram: textos em formato de artigo científico, publicações em português, inglês e espanhol sem limitação de recorte temporal, sendo excluídos, portanto, os demais tipos de formatos textuais como livros, teses, dissertações, resenhas ou artigos que não apresentavam como assunto principal a temáticabuscada.

Primeiramente, foi realizada a busca dos artigos a partir dos descritores (palavras- chave) escolhidos, para, posteriormente, executar a leitura prévia dos títulos e resumos dos mesmos, de forma a identificar e selecionar apenas aqueles relacionados à área de conhecimento abordada. Logo depois, os artigos foram lidos na íntegra entre os dias 6 e 15 de maio de 2018, com objetivo de fazer as articulações e reflexões sobre a discussão do presente trabalho.

A partir da busca inicial por meio dos descritores foram encontrados 33 artigos. Desse total, apenas 18 artigos foram selecionados após a utilização dos critérios de inclusão e exclusão por meio da leitura do idioma, do título e do resumo. Além disso, foram excluídos os artigos que eram duplicados, ou seja, estavam presentes em mais de uma plataforma de busca, e os que não estavam disponíveis de forma gratuita para *download* e leitura na íntegra.

Os dados coletados foram interpretados a partir do método da Análise de Conteúdo da Bardin (2010). Pode ser entendida como uma metodologia de pesquisa usada para descrever e interpretar o conteúdo de toda classe de documentos e textos. A análise de conteúdo se assenta, de modo implícito, na crença de que a "categorização (passagem de dados em bruto a dados organizados) não introduz desvios (por excesso ou por recusa) no material, mas que dar a conhecer índices invisíveis, ao nível dos dados em bruto" (BARDIN, 2010, p. 147).

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A partir da análise os dados foram organizados nas seguintes categorias analíticas: 1. Aumento da degeneração neuronal; 2. Aspectos neuropatológicos; 3. Histopatológicos como uma das causas da etiologia da doença de Alzheimer. Os resultados serão apresentados a partir desses pontos.

## III. Resultados

Os artigos selecionados neste estudo estão veiculados com a língua portuguesa, inglesa e espanhola. Para contemplar esse estudo foram escolhidos 18 artigos publicados no ano de 2018. Ao analisar o delineamento da pesquisa, verificou-se que 15 desses estudos utilizaram- se da abordagem metodológica qualitativa e dois da metodologia mista (qualitativa- quantitativa).

A seguir, apresenta-se o resumo das publicações incluídas na revisão integrativa, com base na distribuição dos estudos.

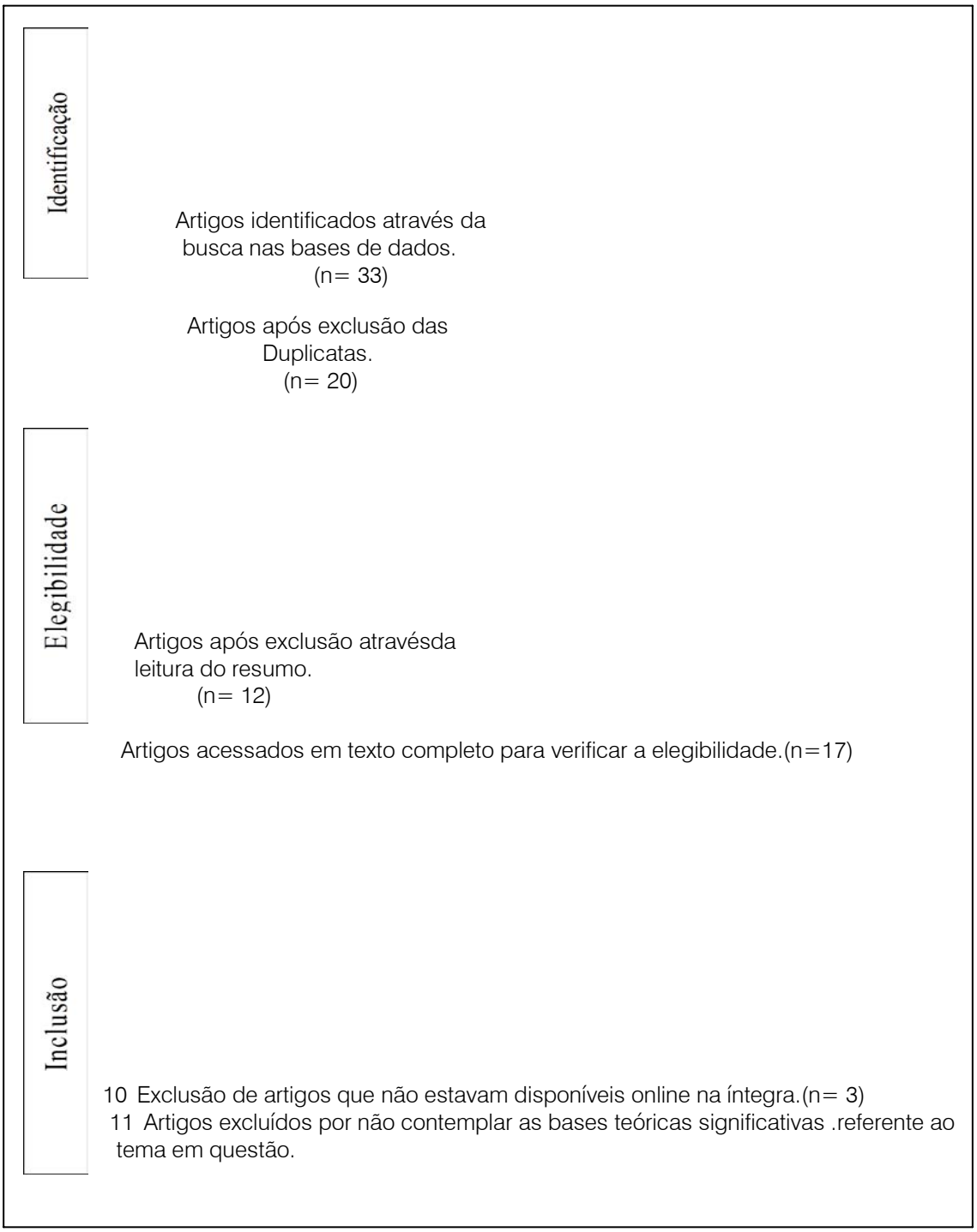


*Figura 1:* Artigos selecionados



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## IV. Discussão

A pesquisa nas bases de dados sinalizou que existem muitos estudos acerca do tema investigado. Conclui-se que os artigos selecionados para essa revisão bibliográfica trazem informações relevantes sobre a relação entre conhecer a degeneração neuronal, e seus aspectos neuropatológicos e histopatológicos, como uma das causas da etiologia da doença Alzheimer.

Observou-se que, apesar de alguns artigos não destacarem, enquanto objetivo principal, a relação estreita entre degeneração neuronal, e seus aspectos neuropatológicos e histopatológicos, como uma das causas da etiologia da doença Alzheime estes contribuíram no embasamento teórico e na coleta de dados sobre degeneração neuronal como uma das causas da etiologia da doença Alzheimer. Além disso, os estudos também permitram compreender a relação entre ambos.

*a) Placas senis e os emaranhados neurofibrilares*

O evento central na patogenia da maioria das demências neurodegenerativas é a agregação anormal de proteínas. Depósitos extracelulares de peptídeo beta-amiloide (Aβ) das placas senis e os emaranhados neurofibrilares neuronais representam marcadores histopatológicos associados à neurodegeneração com deterioração cognitiva em idade avançada. Mais de um século se passou desde sua descoberta e essas características neuropatológicas ainda são reconhecidas como os marcadores principais da doença(BELCAVELLO, 2014).

As características histopatológicas da DA, como placas senis, são produzidas por uma deposição no cérebro humano de fibrilas de peptídeo o b amiloide, um fragmento derivado por processo proteolítico da proteína precursora amiloide, que ativam as células da glia, como a micróglia e os astrócitos, que estão envolvidos na fagocitose dos escombros na área em degeneração, sendo que as placas senis (neuríticas) estão distribuídas em toda parte do córtex cerebral (GUZEN, et. al.; 2010).

As placas senis β-amiloides se desenvolvem primeiro no neocótex seguidas pelo alcéolo e depois pelo suncórtex, e a progressão de sua aparência geralmente corresponde a regiões cerebrais funcional e anatomicamente acopladas 21-23. Os emaranhados neurofibrilares surgem primeiro no locus coeruleus e nas áreas encefinais / límbicas docérebro, e depois se espalham para regiões neocorticais interconectadas.

Desde a descoberta da DA, é reconhecido que os sintomas da doença podem ser associados ao desenvolvimento de inúmeras lesões filamentosas intraneuronais e extracelulares no córtex límbico, assim como no córtex cerebral. Agregados anormais de fibras citoplasmáticas ocorrem tanto nos corpos celulares neuronais, envolvendo os emaranhados neurofibrilares, quanto nos axônios e dendritos. (FALCO et al., 2016).

E, juntamente com a presença das neurites distróficas, há também outro importante sinal histopatológico na DA: a difundida presença de placas e agregados, formados principalmente pelo peptídeo Aβ, na porção extracelular do tecido cerebral, onde existem as diferenças entre um neurônio saudável e um neurônio característico de um paciente com DA.

A explicação da cascata amiloidal teve origem a partir da descoberta da existência de uma variante da doença DA que possuía herança autossômica, a partir de uma mutação no gene que codifica APP e nas presinilinas o que aumenta a produção do peptídeo Aβ, evento suficiente para desenvolver a doença.

E, essa descoberta foi confirmada em 1992, por Hardy e Higgins, quando colocaram as fibrilas insolúveis no peptídeo Aβ como as primeiras espécies tóxicas na doença de Alzheimer, e a formação dos emaranhados neurofibrilares, perda sináptica e morte das células neuronais como um evento secundário. (MENEGHETTI, 2014).

O trabalho que, pela primeira vez, propôs a sequência de eventos denominada "hipótese da cascata amiloide" postulava que o peptídeo Aβ e/ou os produtos de clivagem da sua proteína precursora, uma glicoproteína integral denominada proteína precursora amiloide (APP), são neurotóxicos e podem levar à formação das placas senis, resultando em morte celular.

No cérebro dos sujeitos com a doença do Alzheimer, observa-se grande quantidade de depósitos amiloides, também denominados de placas senis, que se formam por acumulação de um pedaço de proteína peptídeo amiloide na parte externa dos neurônios. (BABALLEYDIER,2017).

As deposições de origem amiloide (peptídeo Aβ) ao serem encontradas em pequenas quantidades em cérebros de idosos sadios, descobriu-se então, que à produção deste tipo de peptídeo era uma das variantes central na patologia da DA.

E essa comprovação foi ainda mais fortalecida, devido à descoberta de que pacientes com trissomia do cromossomo 21 (síndrome de Down) apresentavam também depósitos de Aβ no final da infância ou no início da idade adulta e, posteriormente, desenvolviam as características neuropatológicas clássicas da doença DA, quando atingiam por volta de quarenta anos, devido à localização do gene que codifica a APP, justamente no cromossomo 21 (CORREA 2012).

A hipótese da cascata amiloidal tem recebido suporte a partir de estudos genéticos com casos da forma familiar da doença DA, nos quais mutações tanto na APP quanto nas presenilinas (PS)

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têm mostrado aumento na produção da substância Aβ. (MENEGHETTI, 2014).

A formação do peptídeo Aβ, composto de 40-42 aminoácidos, é o resultado dadigestão da APP, que aparenta ter função fisiológica fundamental com relação aos fenômenos de neuroplasticidade. Observou-se que diversos fragmentos com funções fisiológicas efisiopatológicas são gerados a partir dessa proteína precursora (Rev. Assoc. Med. Bras, 1997). A PPA parece exercer papel importante na facilitação do crescimento neuronal, na sobrevivência da célula e na regulação da atividade da proteína $G_0$, além de sua função reconhecida de adesão entre células e entre o neurônio e matriz cerebral. (Rev. Assoc. Med. Bras, 1997).

A PPA tem características estruturais semelhantes às proteínas de membrana: um extenso seguimento extracelular amino terminal e um curto seguimento intracelular carboxil terminal. As placas senis e o emaranhado neurofibrilar intraneural envolvidos em alterações nos processos neuríticos e células gliais são as características mais importantes na DA (GUZEN, et. al., 2010).

As placas senis são produzidas por uma deposição no cérebro humano de fibrilas de peptideo b amiloide um fragmento derivado por processo proteolítico da proteína precursora amiloide, que ativam células da glia, como a microglia e os astrócitos, que estão envolvidos na fagocitose dos escombros na área em degeneração, sendo que as placas senis (neuríticas) estão distribuídas em toda parte do córtex cerebral (GUZEN, et. al.; 2010).

Assim, as características histopatológicas presentes no parênquima encefálico de pacientes portadores da doença DA incluem depósitos fibrilares amiloidais localizados nas paredes dos vasos sanguíneos, associados a uma variedade de diferentes tipos de placas senis (SERENIKI; VITA., 2008).

Com o advento da microscopia eletrônica, na década de 1960, Michael Kidd e Robert Terry, foram capazes de descrever as lesões ultraestruturais que caracterizam a doença: placas neuríticas e emaranhados neurofibrilares na DA (SELKOE, 2001).

## V. Resultados

*a) Proteína tau e a fosforização dos microtúbulos*

A DA é também caracterizada como uma neuropatologia, devido ao seu marcador, a morte neuronal, teoria esta que prorroga a existência da unidade básica do sistema nervoso, o neurônio. A teoria neuronal foi proposta e formulada nas últimas décadas do século XIX, pelohistologista Santiago Ramon y Cajal (1852 – 1934), que a formulou em oposição à proposta de que o tecido nervoso é constituído por redes contínuas formadas por células nervosas. (FERREIRA, 2017).

Santiago Ramón y Cajal usando a técnica de coloração histológica desenvolvida pelo seu contemporâneo Camilo Golgi, chegou à conclusão de que o sistema nervoso é composto por bilhões de neurônios distintos e que estas células se encontram polarizadas. Ou seja, ele sugeriu que os neurônios em vez de formarem uma teia contínua se comunicam entre si através de ligações especializadas chamadas sinapses. (SABBATINI, 2003).

Santiago Ramon se opôs a Camilo Golgi que defendeu o ponto de vista de que os processos ou neuritos de diferentes células estão fundidos uns aos outros, formando um retículo contínuo, ou rede, semelhante ao que acontece com as artérias e veias do sistema circulatório. De acordo com a explicação reticularista, o encéfalo é uma exceção à teoria celular, a qual afirma que a célula individual é uma unidade de funcional elementar de todos os tecidos animais (CONNORS, et al., 2002).

Os avanços científicos no restante do século XIX levaram à chamada doutrina neuronal, que se estabeleceu graças aos resultados de um trabalho notável desenvolvido pelo anatomista espanhol Santiago Ramon y Cajal (1852-1934), com base nas técnicas histológicas desenvolvidas pelo anatomista italiano Camillo Golgi (1843-1926) (BEAR, et al., 2002).

Outro trabalho de Santiago Ramon, que fundamentou ainda mais a teoria neuronal, foi A lei da polarização dinâmica, que pode ser expressa pelo enunciado "os dentritos transportam impulsos nervosos em direção ao corpo celular (impulsos nervosos celulipetos), enquanto que, os axônios propagam a informação nervosa no sentido de afastamento do corpo celular (sentido celulifigo)" (FERREIRA, 2017).

Assim, ele transformou a hipótese na doutrina do neurônio, confirmando que a unidade individual do sistema nervoso é o neurônio. Mais tarde, a microscopia eletrônica mostrou que uma membrana plasmática envolve completamente cada neurônio, reforçando a teoria de Cajal, e enfraquecendo a teoria reticular de Golgi.

Em síntese, a teoria neuronal pode ser designada pela proposição da existência individualizada das células nervosas (neurônios) e as conexões que suas expansões (dentritos e axônios) estabelecem com outros elementos nervosos por contato.

Mas qual o processo molecular e bioquímico que contribui para o mecanismo da morte neuronal, da perda sináptica, efetuada pela fosforização dos microtúbulos proteína tau?

As proteínas tau são proteínas que estabilizam os microtúbulos, que são estruturas proteicas que fazem parte citoesqueleto nas células, ou seja, são filamentos formados pela polimerização proteínas tubulina e almetralopina. Eles formam um substrato



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onde proteínas motoras celulares (Dineínas e Cinesínas) podem interagir e assim, são usados no transporte intracelullar. (VIKIPÉDIA, 2018).

A Tau tem também como função facilitar a polimerização da tubulina na célula, de maneira que se formem os microtúbulos. Nos emaranhados neurofibrilares a agregação de Tau ocorre pela fosforização irreversível sofrida por essa proteína.

Os microtúbulos são caracterizados por longos filamentos proteicos semelhantes a tubos, e são importantes no momento da divisão celular, locomoção, na morfologia e em outros processos (OLIVEIRA, 2010). Ou seja, como um dos principais componentes do citoesqueleto, os microtúbulos, estão envolvidos na manutenção da morfologia neuronal e na formação dos prolongamentos axonais e dendríticos. (PINHEIRO, 2010).

No que se refere ao sistema nervoso os 27 microtúbulos são componentes importantes nos axônios, onde tem função no transporte de neurotransmissores (SCHMITT et al, 1968).

A proteína Tau foi descoberta em meados dos anos 70 através de estudos sobre fatores necessários para a formação dos microtúbulos. Quando foi possível distinguir que há pelo menos seis espécies moleculares de proteína Tau encontradas em células humanas. O gene que codifica a proteína Tau se encontra no cromossomo 17 e produz um RNAm, que se processa dando lugar até seis isoformas diferentes. (OLIVEIRA, 2012).

Todas estas isoformas da proteína Tau são produtos de um único gene, porém a diferença entre estas seis isoformas se dá pelo processo de splicing durante a transcrição do RNAm (LEE et al., 1988; GOEDERT, et al., 1989) ou por fosforilação em diferentes níveis (ANCOS et al., 1993).

Em 1977 descobriu-se que a proteína tau era uma fosfoproteína e possuía principais funções conhecidas, a sua capacidade de promover a associação e manter a estrutura dos microtúbulos. Estas funções são reguladas pelo seu nível de fosforilação Todavia, a subunidade proteica principal dos emaranhados neurofibrilares/filamentos, só foram identificados como proteína tau e associada a microbutulos, em 1986 por Westem Blot. Pois, neste mesmo ano, demonstrou-se que, na DA, a tau se encontra anormalmente hiperfosforilada e, deste modo, polimerizada em PHF (PINHEIRO, 2010).

Vários estudos demonstraram que a hiperfosforilação reduz a capacidade de a Tau estabilizar os microtúbulos, comprometendo a dinâmica microtubular afetando o transporte intraneuronal, resultando em efeitos deletérios sobre diversos processos celulares. Pois todos os defeitos na proteína Tau alteram o transporte axonal, fatores vitais e necessários para a manutenção da homeostase neuronal (PINHEIRO, 2011).

Além disso, a Tau hiperfosforilada compromete o transporte axonal e o metabolismo das sinapses, causando disfunções que resultam em perda de viabilidade celular, colapso do citoesqueleto microtubular e morte neuronal (GUIMARÃES, 2009).

A hiperfosforilação da Tau favorece a formação de agregados, bloqueando o tráfego intracelular de proteínas neurotróficas e outras proteínas funcionais, e resultando em perda ou declínio no transporte axonal ou dendrítico nos neurônios.

Estudos cinéticos in vitro demonstram que os resíduos Ser 199/202 estão entre os locais de fosforilação críticos da proteína Tau, onde convertem a molécula Tau a uma molécula que sequestra outras proteínas Tau formando os emaranhados neurofibrilares (ALONSO, et al., 2004).

Evidências experimentais indicam que a excitação de receptores colinérgicos muscarínicos está associada à fosforilação da proteína Tau. A ativação destes receptores resulta em ativação de uma proteína quinase C, que por sua vez conduz à inativação da proteína quinase GSK-3, responsável pela fosforilação da proteína Tau (CALIMAN et al., 2005).

Quando fosforilada por quinases, a proteína tau se desliga do microtúbulo, desestabilizando-o e promovendo a morte neuronal. (adaptado de http://www.emdmillipore.com/html/cbc/alzheimers_disease_tau_antibodies_proteins.htm).

Sendo assim, a proteína Tau, na sua forma hiperfosforilada, não funciona para a célula, pois é tóxica para o ambiente celular e teria que ser reparada (desfosforilada) ousujeita a degradação.

A fosforilação da Tau, em seus sítios específicos de ligação é o que garante seu funcionamento normal (MONTEIRO et al., 2011), sendo que sua fosforilação inapropriada resulta em disfunção e menor viabilidade celular. Segundo Lee et al. (2001) e Monteiro et al. (2011), todas as doenças neurodegenerativas envolvidas com a proteína Tau apresentam esta proteína anormalmente fosforilada. Evidências experimentais indicam que a excitação de muscarínicos está associada à fosforilação da proteína Tau. A ativação destes receptores resulta em ativação de uma proteína quinase C, que por sua vez conduz à inativação da proteína quinase GSK-3, responsável pela fosforilação da proteína Tau (CALIMAN et al., 2005).

## VI. Discussão

*a) A enzima acetilcolinesterase e a degeneração neuronal*

Um dos episódios mais interessantes da história das Neurociências é o de Otto Loewi, que trabalhando na Áustria na década de 1920, onde mostrou definitivamente que a transmissão sinâptica entre o nervo e o coração é mediada quimicamente. O



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coração recebe dois tipos de inervaçâo: um aumenta o batimento cardíaco e outro o diminui. O último tipo de inervaçâo é feito pelo nervo vago. Loewi isolou um coração de rã com a inervaçâo vagal intacta, estimulou o nervo eletricamente e observou separadamente a redução dos batimentos cardíacos. A demonstração crucial de que este efeito era mediado quimicamente veio quando Loewi pegou a solução que banhava o coração e a aplicou sobre o outro coração isolado, observando a redução do batimento deste também. A ideia para este experimento ocorreu a Loewi em um sonho, como ele mesmo conta (PARADISO, et. al., 2002).

"Na noite de domingo de Páscoa, em 1921, acordei, acendi a luz e fiz algumas anotações em uma pequena tira de papel. Então adormeci novamente. Às 6 horas da manhã ocorreu-me que eu havia escrito alguma coisa muito importante, mas não fui capaz de decifrar os rabiscos. Aquele domingo foi o mais desesperado dia em toda a minha vida científica. Na noite seguinte, porém, acordei às 3 horas e lembrei o que era. Dessa vez, não corri nenhum risco: fui imediatamente ao laboratório fazer o experimento com corações de rãs, conforme descrito, e às 5 horas da manhã a transmissão química do impulso nervoso estava conclusivamente provada Uma consideração mais cuidadosa durante o dia rejeitaria, sem dúvida, esse tipo de experimento que executei, porque pareceria muito improvável que, se o impulso nervoso liberasse um transmissor químico, ele o fizesse não apenas em quantidade suficiente para alterar o órgão efetor, neste caso, o coração, mas, de fato, o fizesse em tal excesso que ele poderia escapar parcialmente para o fluído que banhava o coração, podendo, portanto, ser detectado. Apesar de todo o conceito noturno do experimento ser baseado nessa eventualidade, o resultado provou ser positivo, contrariando a expectativa (LOEWI, 1953 p.33,34).

O composto ativo, ao qual Loewi chamou vagusstoff (algo assim como "vagoessência"), veio a ser a acetilcolina. A acetilcolina é também o neurotransmissor nas sinapses entre os nervos e os músculos esqueléticos. Aqui diferentemente do efeito no coração, a acetilcolina causa excitação e contração do músculo (BEAR, 2002). A acetilcolina (ACo) é o transmissor na junção neuromuscular e, portanto, sintetizado por todos os neurônios motores na medula espinhal e no tronco encefálico.

Assim, a primeira molécula identificada como um neurotransmissor por Otto Loewi, em 1920, foi a acetilcolina ou ACo. Para descrever as células que produzem e liberam ACo, o farmacologista Henry Dale introduziu o termo colinérgico. Dale denominou noradrenérgicos os neurônios que usam o neurotransmissor aminérgico noradrenalina (NA, também denominada norepinefrina). A conversão de usar o sufixo érgico continuou quando os transmissores adicionais foram identificados. (BARLOW, et. al., 2002).

Em 1936, Henry Dale e Otto Loewi partilharam um prémio Nobel pela investigação pioneira sobre a neurotransmissão química e em particular pela descoberta e caracterização funcional do primeiro neurotransmissor identificado, a ACh.

Vários são já os neurotransmissores conhecidos, mas o primeiro a ser descoberto no cérebro foi a Acetilcolina, e também no sistema nervoso periférico. Este neurotransmissor está associado à aprendizagem e à memória. Uma vez produzida, a ACh é armazenada em células cerebrais e libertada na fenda sináptica através de um estímulo. Na DA, verifica-se uma diminuição de ACh disponível devido a uma diminuição da sua síntese (PINHEIRO, 2011)

A Colina-O-Acetil-Transferase (ChAT) é uma enzima responsável pela síntese da Ach a partir de acetil-coezima e colina. A glicerofosforilcolina, a fosforilcolina e a fosfatidilcolina geram a colina que é utilizada como substrato e transportada para o SNC através da circulação sanguínea. Assim, as fontes de colina para a síntese de Ach provêm da circulação, além da sua recaptação após a liberação e degradação desse neurotransmissor (VENTURA 2009).

Em 1914, Dale classificou as ações da Ach em muscarínicas e nicotínicas. Essa classificação foi baseada nos subtipos de receptores colinérgicos capazes de se ligar à nicotina e à muscarina, respectivamente, e que respondem à ativação colinérgica com alta afinidade. (BEAR, et. al., 2009).

A maioria das eferências colinérgicas, partes do prosencéfalo basal, área formada por centenas de neurônios localizados nos núcleos septal medial, banda diagonal, substântia innominata basal de Meynert (TELES, 2015).

E são eles que fornecem a intervenção colinérgica para o hipocampo, e o núcleo basal de Meynert, que provê a maior parte da inervação colinérgica para o neocórtex, que se projetam para o hipocampo, neocórtex, partes do córtex límbico e amígdala modulando as funções cognitivas (CONNORS, 2002).

Segundo (BEAR et. al.; 2002), existem dois importantes sistemas colinérgicos modulatórios de projeção difusa no encéfalo, um dos quais é chamado complexo prosencéfalo basal; e o segundo é o de complexo pontomesencefalo-tegmental, onde estão incluídas as células da ponte e do tegmento mesencéfalo que utilizam ACo. (PARADISO, et. al.; 2002).

Assim como os sistemas noradrenérgico e serotoninérgico, o complexo prosencefálico basal também pode ter um papel especial no aprendizado e na formação da memória. (BEAR, 2002).



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Ainda segundo BEAR. et, al.; 2002), o segundo sistema denominado de complexo pontomesencefalo-tegmental, é responsável pela inclusão das células da ponte e do tegmento mesencefálico que utilizam ACo. Este sistema atua principalmente no tálamo dorsal onde, juntamente com os sistemas noradrenérgico e serotoninérgico, regula a excitabilidade de núcleos re-transmissores ou relés sensoriais. (CONNORS, 2002).

E o interesse por essas regiões, de acordo com (PARADISO, et. al.; 2002) tem sido impulsionado pela descoberta de que são nestas regiões que estão as primeiras células a morrer durante a evolução da DA, que é caracterizada por uma perda progressiva e profunda das funções cognitivas (BEAR, et.al., 2002).

A importância da função colinérgica nos processos de aprendizagem e memória é conhecida desde o início da década de 70, e as pesquisas a respeito da importância do sistema colinérgico na DA demonstraram diversas características, como a diminuição na concentração da colina acetiltransferase (ChAT), enzima responsável pela síntese da acetilcolina (ACh), no córtex e no hipocampo, assim como uma redução variável dos neurônios colinérgicos localizados no núcleo basal de Meynert. (DAVIS, et. al., 2016).

Foi a descoberta inicial da neurotransmissão colinérgica que conduziu à "Hipótese Colinérgica", elaborada por vários investigadores. (Esta hipótese abrange várias funções cerebrais e disfunções, desde desordens afetivas, como a depressão, a esquizofrenia, e o delírio, à regulação do sono e danos cerebrais traumáticos PINHEIRO, 2011).

Isto ocorreu durante os anos 70 e 80, quando a ideia anterior foi aplicada à examinação de amostras do cérebro de doentes com DA, e assim a Hipótese Colinérgica atingiu o seu auge. Esta hipótese sugere que a perda selectiva de neurônios colinérgicos naDA resulta de um défice relativo da ACh em regiões específicas do cérebro que medeiam as funções de aprendizagem e memória.

Neurônios colinérgicos também produzem a enzima acetilcolinesterase (ACoE), degradadora de (ACo) . A (ACoE) é secretada na fenda sináptica e está associada às membranas dos terminais axonais colinérgicos.

A ACoE degrada ACo em colina e ácido acético. Isto acontece muito rapidamente,pois a ACoE possui uma das taxas catalíticas mais rápidas dentre as enzimas conhecidas (PINHEIRO, 2011).

Assim, a ACoE, sendo o alvo de muitos gases neurotóxicos e inseticidas, inibi a ACoE, gerando a quebra da ACo, prejudicando a transmissão em sinapses colinérgicos, e em muitos casos, provocando a diminuição significativa desta enzima com a idade, associando-se a perda neuronal.

## VII. Considerações Finais

Os estudos e as pesquisas têm avançados na direção da busca da compreensão e do entendimento sobre os mecanismos histopatológicos e neuropatológicos da DA, e mesmo assim, a explicação da degeneração neuronal como uma das causas da DA, ainda sofre muita incompreensão no campo da ciência.

Todavia, os achados da revisão de literatura delimitada neste artigo, demonstraram que, desde a descoberta da DA, em 1906, por Aloís Alzheimer, depois de um século ter se passado, essas características histopatológicas e neuropatológicas ainda são reconhecidascomo os marcadores principais da doença.

E a perpetuação desses marcadores, atualmente, tem vindo principalmente do campo da neurociência, através de pesquisas e das técnicas do campo da imagiologia. E um dele é o exame precoce que é o de análise do líquido cefalorraquidiano, para identificar a presença de beta amilóides ou da proteína tau, tanto do total de proteínas como a concentração tau fosforizadas, pois este exame proteico, realizado através da punção lombar, pode prever o aparecimento de Alzheimer com sensibilidade entre 94 e 100%.

Sendo a DA, uma doença grave de comprometimento cerebral das funções cognitivas e comportamentais, considerando que, atualmente, não existem evidências conclusivas que permitam apoiar qualquer medida em concreto para a prevenção do Alzheimer, embora os fatores de riscos cardiovasculares, como a hipercolesterolemia, hipertensão arterial, diabetes ou tabagismo estejam associados a um maior risco de desenvolver a DA, o tratamento não diminui a DA.

Em 1906, Alois Alzheimer deixou o seu legado, e já se passou um século, projeções de prevalência e incidência indicam que ocorrerá um crescimento mais elevado do número de pessoas com demência no mundo. Estima-se que o número total de pessoas que sofrem de demência mundial é de 35,6 milhões e é previsto que este número quase dobre a cada 20 anos – para 65,7 milhões em 2030 e 115,4 milhões em 2050. Por isso, justificam-se os estudos sobre a referida temática, para que a ciência continue sendo atraída, através de pesquisas e estudos, para validação e represente um novo alvo, para a compreensão da DA, sua prevenção, aperfeiçoamento de diagnóstico precoce, tratamento eficaz e sua cura.

## References Références Referencias

1. ALBERTS, BRUCE. A biologia molecular da célula. Disponível no site: http://www.ncbi.nlm.nhi.gov.pubmed/20458069. São Paulo, acesso em 15 de maio de 2018.



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2. ALMEIDA, O. P. Biologia molecular da doença de Alzheimer: uma luz no fim do túnel? Rev. Assoc. Med. Bras. São Paulo, vol.43 n.1. p. 77-81. Jan./Mar. 1997.
3. BARLOW, D. H.. DURAND, V. M.; Demência do tipo de Alzheimer. In: . Psicopatologia: Uma Abordagem Integrada. 2. ed. São Paulo: Cenagage, 2008. p. 23 – 133; 141 - 159; 497 – 517; 631-644.
4. BARRETO, D. L. T.; SOUZA, N. M. T.; BARROSO, B.; NOGUEIRA, D. R. A Doença de Alzheimer e seus efeitos fisiológicos no organismo. Anais Cieh. João Pessoa, v. 2, n. 1. p.1-7, 2015.
5. BARDIN, Laurence. Análise de conteúdo. 4ª. ed. Lisboa: Edições 70, 2010.
6. BEAR, M. F; CONNORS, B. W.; PARADISO, M. A. Neurônios e Glia. In: . Neurociências Desvendando o Sistema Nervoso. 2. ed. Porto Alegre: Artmed, 2002, p. 23 – 37.
7. BELCAVELLO, L. Estudo genético e de instabilidade genômica da doença Alzheimer em pacientes de Vitória – ES. 94f. Tese (Doutorado Biotecnologia, ênfase em saúde.). Universidade Federal Do Espírito Santo. Rede Nordeste de Biotecnologia, Vitória – ES, 2014
8. DALGALARROMBO, P. Demências. In: Psico-patologia e Semiologia dos Transtornos Mentais. 2. ed. Porto Alegre: Artmed, 2008, p. 376 – 388.
9. DE FALCO, A. D; CUKIERMAN, D. S.; DAVIS, R. A. H.; REY, A. N. Doença de Alzheimer: Hipóteses etiológicas e perspectivas de tratamento. Rev. Química Nova. Rio de Janeiro, v. 39, n. 1. p. 63-80, 2016.
10. DE SOUZA, L. C.; TEIXEIRA, A. L. Neuropsicologia das demências. In: FUENTES, D.; DINIZ, L. F. M.; DE CAMARGO, C. H.; COSENGA, R. M. Nuropsicologia teoria e prática (org.). 2. ed. Porto Alegre: Artmed, 2014, p. 321 – 330.
11. DAMÁSIO, A. R. A revelação do cérebro de Gage. In: O erro de Descartes: emoção, razão e o cérebro humano. 3. ed. São Paulo, 2012, p. 39 – 87.
12. FERREIRA, F. R. M. A teoria neuronal de Santiago Ramon y Cajal. 419f.Tese (Doutorado em Psicologia) – Instituto de Psicologia da Universidade de São Paulo, 2013.
13. FRIDMAN, C; GREGÓRIO P. S.; DIAS NETO. E; OJOPI, E. P. B. Alterações genéticas na doença de Alzheimer. Revista de Psiquiatria Clínica. São Paulo, v. 31, n.1, p. 19-24, 2004.
14. GUZEN, P. F.; CAVALCANTI, P. L. R. J. Influência das Proteínas Beta Amiloide e Tau na doença de Alzheimer. João Pessoa, Facene/Famene 10(1): 57-60, 2010.
15. LIMA, T. Z. Estudos sobre a patogênese e tratamento da Doença de Alzheimer. 93f. Tese (Doutorado) - Universidade Federal de São Paulo (UNIFESP), São Paulo, 2010.
16. KREUTZ, F. Efeito do Peptídeo B-Amiloide sobre a Biossíntese de Gangliosídios e Avaliação da Atividade Neuroprotetora do GM1. 62f. Dissertação (Mestrado em Ciências Biológicas) – Universidade do Rio Grande do Sul, 2010.
17. LIMA, T. Z. de. Estudos sobre a patogênese e tratamento da Doença de Alzheimer. 2010. 93 f. Tese (Doutorado) - Universidade Federal de São Paulo (UNIFESP), São Paulo, 2010.
18. LUCIANO, B. Estudo genético e de instabilidade genômica da doença Alzheimer em pacientes de Vitória – ES. 94f. Tese (Doutorado em Biotecnologia com ênfase em saúde). Universidade Federal do Espírito Santo, Vitória, 2014.
19. MARTELLIA, A; MARTELLIB. F.P. Alterações Cerebrais e Análise Histopatológica dos Emaranhados Neurofibrilares na Doença de Alzheimer. São Paulo. UNICIÊNCIAS, v. 18, n. 1, p. 45-50, Jun. 2014
20. MENEGHETTI, A. B. Avaliação dos Mecanismos envolvidos na Toxicidade de Oligômeros do Peptídeo B-Amiloide em Cultura Organotípica de Hipocampo de Ratos. 82f. Dissertação (Mestrado em Bioquímica) – Universidade Federal do Rio Grande do Sul, 2014.
21. OJOPI, E. P.B.; BERTOCINI, A.B. DIAS NETO, E.; Apolipoproteína E e a doença de Alzheimer. Revista de Psiquiatria Clínica. São Paulo. v. 31. n. 1. p. 26-33, 2004.
22. OLIVEIRA, A, S. A de. Efeito modulatório dos receptores nicotínicos sobre a degradação de isoformas tóxicas da proteina tau: importância para a doença de Alzheimer. 91f. Dissertação (Mestre em Biossistema). Universidade do ABC, Santo André, 2012.
23. PAULA, V. J. R; GUIMARÃES, F. M.; FORLENZA, O. V. Papel da proteína Tau na fisiopatologia da demência frontotemporal. São Paulo. Revista de psiquiatria clínica. vol.36 n. 5, 2009.
24. PEREIRA, P. M. C. M. Doença de Alzheimer: Perspectivas de tratamento. 38f. Dissertação (Mestrado em Medicina) – Universidade da Beira Interior Ciências da Saúde, Covilhã, 2013.
25. PINHEIRO, S. I dos S. Efeito do óxido na proteína tau: implicação na doença de Alzheimer. 62f. Dissertação (Mestrado em Bioquímica). Universidade da Beira Interior Covilhã, 2010.
26. PINHEIRO, S. M. M. Desenvolvimento de métodos para estudo de inibidores da acetilcolinesterase (Tratamento sintomático da Doença de Alzheimer). 82f. Dissertação (Mestrado em Bioquímica). Universidade de Lisboa. Faculdade de Ciências. Lisboa, 2011.
27. RIBEIRO, C. F. Doença de Alzheimer: A principal causa de demências nos idosos e seus impactos na vida dos familiares e cuidadores. 59f. TCC




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(Curso de especialização em atenção básica na saúde da família) – UFMG, Belo Horizonte, 2010.

28. SERENIKIL, A.; VITAL, M. A. B. F.; A doença de Alzheimer: aspectos fisiopatológicos e farmacológicos. Revista de Psiquiatria. Curitiba, v. 30, n.1 suplemento. 2008.
29. TELES, M. Relação entre o sistema colinérgico e a formação cognitiva após treino semanal de atenção em camundongos infundidos cronicamente com peptídeo de B- amiloide. 58f. Dissertação (Mestre em Farmacologia). Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo, 2015.
30. SANTOS, F. M. C. S.. A doença de Alzheimer: a importância da neuropatia da doença. 69f. Tese (Mestre em Ciências Farmacêuticas). Universidade do Porto, 2011.
31. SOUZA, L. C; TEIXEIRA, A. L. Neuropsicologia das Demências. In. Fuentes, D. de. Neuropsicologia: Teoria e Prática (org.). 2. ed. Porto Alegre: Artmed, 2014, p. 321 – 329.
32. VENTURA, L. M.; ABREU, P. A.; FREITAS, R. C. C.; SATHLER. P. C.; LOUREIRO, N.; CASTRO, H. C. Sistema colinérgico: revisitando receptores, regulação e a relação com a doença de Alzheimer, esquizofrenia, epilepsia e tabagismo. (2009).
33. ZAINAGHI, I. A. Fosfolipase A2, fluidez de membrana e proteína precursora do amiloide em plaquetas na doença de Alzheimer e Comprometimento Cognitivo Leve. 89f. Tese (Doutorado em Ciências) – Faculdade de Medicina da Universidade de São Paulo, São Paulo, 2006.



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# Computed Tomography in the Assessment of Cardiac Adipose Tissue and Coronary Artery Atherosclerosis

By N.M. Djuraeva, A.I. Ikramov, M.F. Maksudov, Kh.V. Abdukhalimova & Khaybullina Z.R

*Abstarct-* This study examines the relationship between atherosclerotic lesions of the coronary arteries and quantitative indicators of epicardial adipose tissue according to MSCT data. Overall, 96 patients were investigated who were admitted to the hospital during 2019-2020 years, with a diagnosis and suspicion of coronary artery disease, who were examined and treated at the State Institution Republican Specialized Scientific and Practical Medical Center for Surgery named after Academician V. Vakhidov. Of the 96 patients, there were 51 men and 45 women; the age of all patients was over 45 years old (59.75±0.9 years). Based on the results of MSCT angiography, the patients were classified according to the degree of stenosis using the CAD-RADs system. The thickness, area, and volume of epicardial adipose tissue (EAT) were determined in all patients. A direct correlation of average strength between the volume of EAT and the degree of coronary atherosclerosis ($r=0.59$) ($p<0.05$) was established, as well as weak direct relationship between the degree of stenosis and the area of pericoronary adipose tissue ($r=0.24$), ($p<0.05$).

*Keywords:* *MSCT angiography, coronary arteries, epicardial adipose tissue, paracardial adipose tissue.*

*GJMR-F Classification:* *NLMC Code: WG 595*

*Strictly as per the compliance and regulations of:*

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# Computed Tomography in the Assessment of Cardiac Adipose Tissue and Coronary Artery Atherosclerosis

N.M. Djuraeva [α], A.I. Ikramov [σ], M.F. Maksudov [ρ], Kh.V. Abdukhalimova [ω] & Khaybullina Z.R [¥]

*Abstract-* This study examines the relationship between atherosclerotic lesions of the coronary arteries and quantitative indicators of epicardial adipose tissue according to MSCT data. Overall, 96 patients were investigated who were admitted to the hospital during 2019-2020 years, with a diagnosis and suspicion of coronary artery disease, who were examined and treated at the State Institution Republican Specialized Scientific and Practical Medical Center for Surgery named after Academician V. Vakhidov. Of the 96 patients, there were 51 men and 45 women; the age of all patients was over 45 years old (59.75±0.9 years). Based on the results of MSCT angiography, the patients were classified according to the degree of stenosis using the CAD-RADs system. The thickness, area, and volume of epicardial adipose tissue (EAT) were determined in all patients. A direct correlation of average strength between the volume of EAT and the degree of coronary atherosclerosis (r=0.59) (p <0.05) was established, as well as weak direct relationship between the degree of stenosis and the area of pericoronary adipose tissue (r=0.24), (p<0.05).

*Keywords: MSCT angiography, coronary arteries, epicardial adipose tissue, paracardial adipose tissue.*

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## I. Introduction

According to the results of the Framingham Heart Study, the Multi-Ethnic Study of Atherosclerosis, and the Nurses Health Study, obese patients had double times higher risk of developing heart failure (HF), and the progression of cardiovascular diseases was 4.1 times higher compared with persons with average weight [2, 3]. According to the ESSE study, obesity is the third leading risk factor for CVD after dyslipidemia and hypertension. It has been shown that people suffering from abdominal obesity, having the same waist circumference, may differ markedly in the presence of cardiometabolic risk factors. In addition to the total amount of adipose tissue in the body, its distribution is significant - it is the visceral adipose tissue. According to the results of numerous studies, it is recognized as a pathogenetic platform for the development of metabolic disorders, atherosclerotic vascular lesions, and CVD [3, 17, 19, 20]. The widespread introduction of radiological diagnostic methods has made it possible to classify obesity into visceral (VO) and subcutaneous (SC), depending on the location of excessive fat accumulation. A wealth of scientific and medical evidence suggests that VO is associated with an increased risk of morbidity and mortality from CVD, including stroke, congestive heart failure, and myocardial infarction.

Accumulation of fat in the visceral region is not the only metabolically active fat depot; at least six more regional depots are characterized by similar disorders against the background of chronic inflammation [1]. More and more data on the effect of epicardial fat depots (EFD) on the risk of developing cardiovascular pathology [3, 4, 5]. Currently, the study of not only abdominal obesity but also other ectopic fat depots, such as EFD and perivascular fat, has become relevant since their close relationship with the degree of atherosclerotic lesions of the coronary arteries has been revealed [3].

As can be seen from these data, the historical concept of the relationship between obesity and cardiovascular disease (CVD) has changed in recent years, considering the emerging new results from prospective studies.



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EAT is fatty tissue located between the myocardium and the visceral pericardium, while paracardial fat is located outside the heart. Epicardial and paracardial adipose tissue targets in-depth studies due to their close topographic and anatomical location to the coronary arteries and myocardium (Fig. 1).

a b

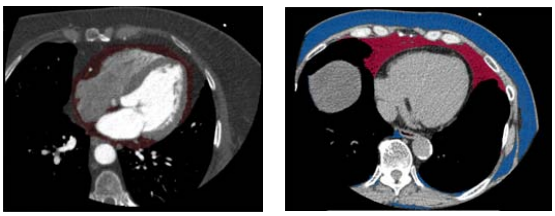

*Figure 1:* (a) Epicardial adipose tissue (b) pericardial adipose tissue on axial MSCT tomograms.

The study of the relationship between the volume of EAT and the state of the coronary arteries (CA) in patients with coronary artery disease can be essential for predicting the course of CVD. The study of the diversity of pathogenetic mechanisms of increasing the risk of CVD development due to the summation of the effects of a fat depot on CA atherogenesis is a promising area of preventive cardiology. In this regard, the purpose of this study was to assess the amount of EAT using volumetric MSCT and to study the correlation of this indicator with the degree of atherosclerotic lesions of the coronary artery.

## II. Material and Methods

We examined 96 patients with coronary artery disease, angina pectoris of FC II and III, who were admitted for examination and treatment at the State Institution "RSPMTSH named after Academician V. Vakhidov" in the period from 2019 to 2020. The average age was 59.72±1.58 years; 51 (53%) men and 45 (47%) women.

MSCT was performed on the “Aquillion one” apparatus of the “Genesis” version (Toshiba, Canon), which allows the study to be carried out in a 640-section mode. Patients underwent native scanning, MSCT angiography of CA, as well as non-contrast MSCT study with determination of the volume and thickness of the EAT, the area of epicardial (paracoronary) and paracardial fat using a particular protocol Fat measurement, with obtaining data on the visceral fat depot.

Volume MSCT angiography of CA was performed after intravenous injection of 50-70 ml of contrast medium (CM) at a rate of 4-6 ml/s. Were used β-blockers to reduce the pulse to the required level - 60-70 beats per minute. Patients with renal insufficiency, severe calcification and multiple stents of the coronary arteries were excluded from the study.

All studies were interpreted by two radiologists using the original axial image. The datasets have been converted and retrieved from the Vitrea workstation. Coronary cross-sections were generated and transformed into curvilinear multi-plane MPR, MIP and VR reconstructions. The severity of coronary atherosclerosis was classified as hemodynamically significant and insignificant location of coronary artery stenosis according to the standardized CAD-RADs system (the first group - CAD-RADs 1,2 and the second group - CAD-RADs 3,4). The average sizes of CA stenosis were determined at points free from atherosclerotic lesions.

All changes in the volume and thickness of the EAT were made in the most static phase of the cardiac cycle - in the mid-diastolic phase of the cardiac cycle by 70-80% of the R-R interval.

The measurement of the EAT thickness was carried out in the projection s/3 RCA, d/3 LAD at the level of the interventricular septum and along the lateral wall of the right ventricle (Fig. 2), taking into account the average value of all measurements.

The area of EAT was calculated at the basal level of the ventricles of the heart along the short axis, as well as the area of adipose tissue of the pericoronary region at the level of the left coronary artery (LCA) trunk, n/3 of the anterior interventricular branch (AIVB) and n/3 of the right coronary artery (RCA) with manual designation of the locus of interest and automatic measurement of the EAT area.

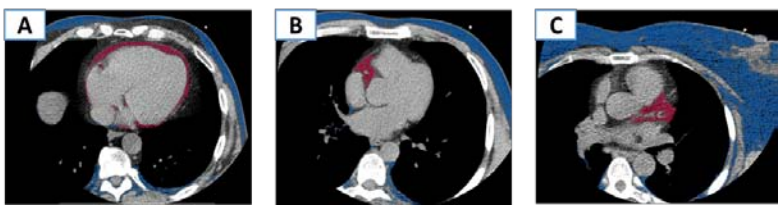


*Figure 2:* Determination of the area of EAT at the level of the basal parts of both ventricles along the short axis (A), determination of the area of pericoronary fat at the level of p/3 RCA (B), the trunk of the LCA and p/3 AIVB (C).



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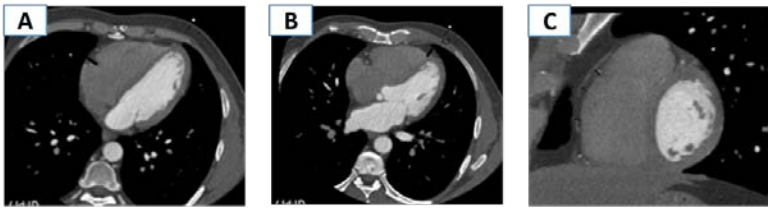


*Figure 3:* Determination of EAT thickness: maximum distance at the level with / 3 RCA (A), at the level of the ventricular septum (B) and along the lateral wall of the right ventricle (C).

The volume of EAT was calculated by MSCT angiography of CA using the "Fat measurement" option. Produced targeted isolation of EAT in the density range of -150-70 HU, followed by manual correction of the epicardial boundaries and automatic determination of adipose tissue volume in a given area with a 3D reconstruction of the total volume. Statistical analysis of the data obtained was carried out using the Stattech software package.

## III. Results

In patients with coronary artery disease, the following quantitative indicators were analyzed: thickness, area and volume of EAT. The severity of atherosclerotic lesions was judged by the degree of coronary artery stenosis, as well as the number of affected coronary arteries.

It was found that the average value of the EAT volume in hemodynamically insignificant (HDIS) stenoses was 131 ± 6.81 $mm^3$, and in hemodynamically significant (HDS) stenoses - 198 ± 13.8 $mm^3$ ($p < 0.05$). The thickness of the EAT at the level of s / 3 RCA with HDIS stenosis was 14.7 ± 0.75 mm, and with HDS stenoses 15.5 ± 0.58 mm ($p > 0.05$), the thickness of the EAT at the level of the free wall of the RV in HDIS stenosis was 5.32 mm ± 0.33 mm, and with HDS stenoses 5.11 ± 0.39 mm ($p > 0.05$), the thickness of the EAT at the level of d / 3 AIVB in HDIS stenosis was 5.02 ± 0.33 mm, and with HDS stenoses 6.29 ± 0.39 mm ($p < 0.05$), while it was revealed that with HDS stenoses, thickness <5 mm was detected in 70% of patients, and with HDS stenoses> 5 in 83 % of patients ($p < 0.05$).

The area of EAT at the level of both ventricles with HDIS stenoses was 7.5±0.51 $cm^2$, and with HDS stenoses this area was 8.36 ± 0.65 $cm^2$ ($p < 0.05$), and in 87% of patients it was > 7 $cm^2$. The pericoronary area of the EAT with HDIS stenosis was 7.34 ± 0.86 $cm^2$, in this group <7 $cm^2$ was found in 69% of patients, and with HDS stenoses this area was 9.23±1.12 $cm^2$ ($p<0.05$). When comparing the area of paracardial adipose tissue (PAT) with HDIS stenoses was 14.7±1.58 $cm^2$, and with HDS stenoses 17.4±2.47 $cm^2$ ($p < 0.05$).

Analysis of the correlation between the volume of EAT and the age of patients showed that the correlation coefficient was r=0.02, i.e., there was no connection between these indicators. This indicates that the severity of the atherosclerotic process in the vessels largely depends on several other controllable and uncontrollable factors.

Neveen I. Samy and others did not reveal statistically significant correlations between the thickness of the EAT and such risk factors as smoking, dyslipidemia, hypertension, obesity; according to their data, the correlation of these risk factors with the thickness of pericoronary adipose tissue was statistically insignificant [12].

Analysis of the relationship between the volume of EAT and the severity of CA atherosclerosis (hemodynamically insignificant and significant areas of stenosis) showed the presence of a significant direct correlation of average strength (Fig. 4).



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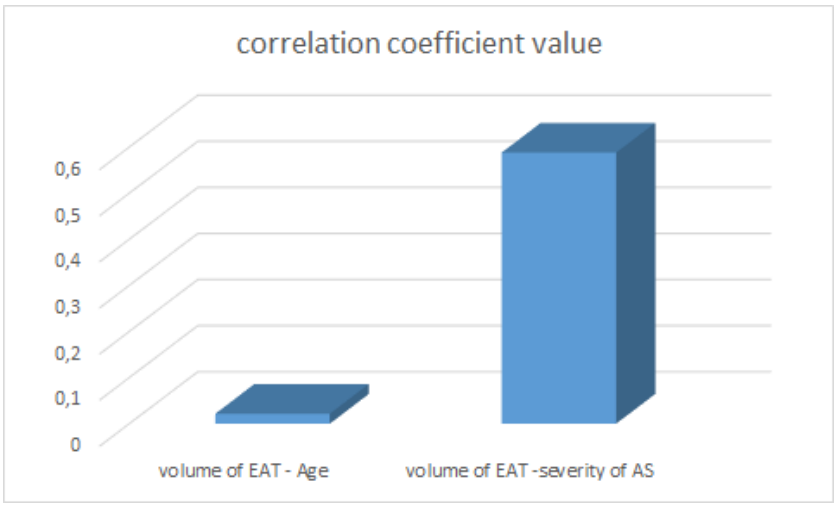


*Figure 4:* The results of the correlation analysis of the indicators of the volume of EAT, age and severity of AS CA.

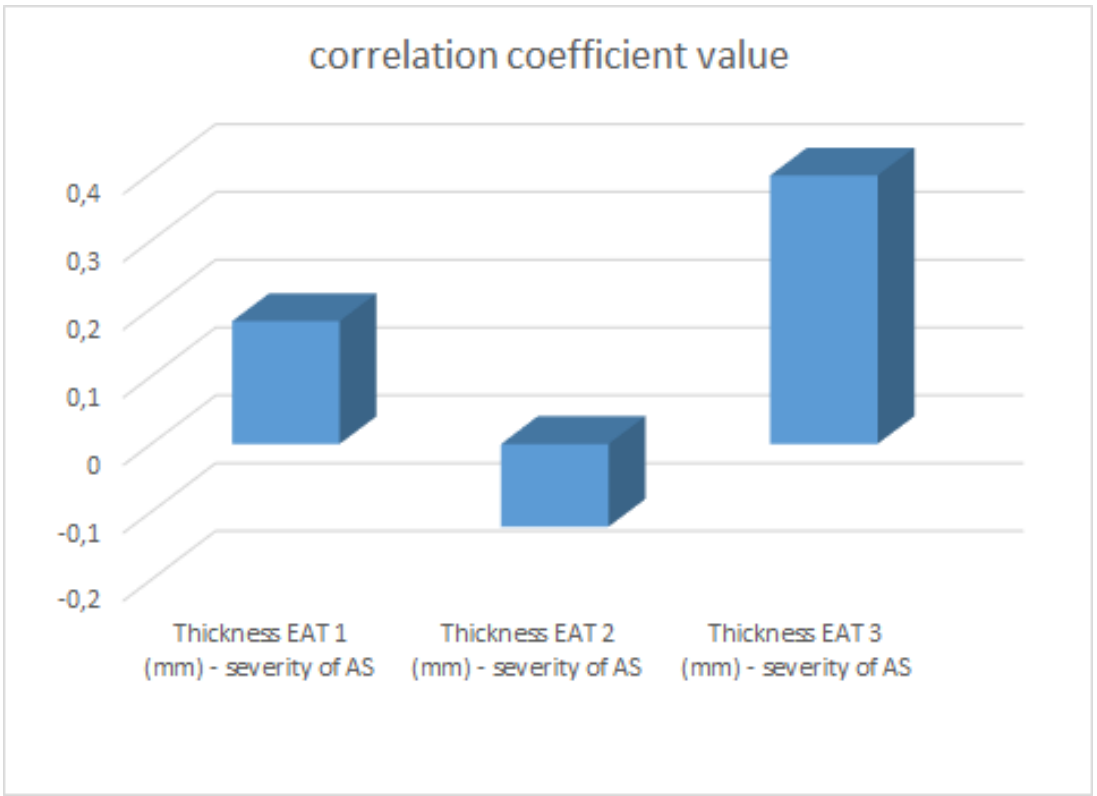


*Figure 5:* The results of the correlation analysis of the indicators of the EAT volume, estimated in 3 types of measurements. The thickness of the EAT 1 is the distance between the myocardium and the visceral epicardium at the level of s/3 RCA, the thickness of the EAT 2 is at the level of the free wall of the RV, the thickness of the EAT 3 is at the level of d/3 AIVB.

Correlation analysis between the data on the EAT thickness with the CA severity index showed that the most significant relationship was found between the EAT thickness measured at the level of d/3 AIVB, that is EAT-3 at r=0396.

It is noteworthy that when assessing the correlation between the area of the EAT (at the level of the ventricles) and the severity of AS CA (HDIS, HDS areas of stenosis), it was found that the correlation coefficient was negative (r=-0.161), and in the ratio of the areas of pericoronary and paracardial AT, the correlation was positive and significant (r=0.238, r=0.197).

It is clearly demonstrated by MSCT tomograms with 3D reconstruction of the EFT, where its boundaries are traced on axial sections and 3D reconstruction of the CA.



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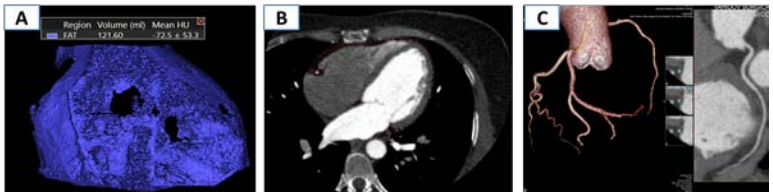


*Figure 6:* 53-year-old female patient. 3D - volumetric image of EAT with the determination of the total volume (A), axial projection with the designation of the boundaries of the epicardial fat depot (B), curvilinear reconstruction of the CA without areas of stenosis (C).

## IV. Discussion

A lot of research in the USA – Rosito and others [15], Mahabadi and others [14], Ding and others [8] - and in Japan - Ito and others [11] - showed that the volume of EAT is an independent predictor of the severity of coronary atherosclerosis, correlates with the degree of coronary artery disease. At the same time, the methodology for determining the area and volume of EAT is different.

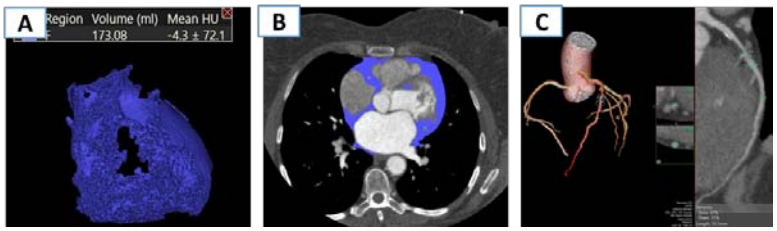


*Figure 7:* 60-year-old female patient. 3D - volumetric image of EAT with determination of the total volume (A), axial projection with designation of EAT boundaries (B), curvilinear reconstruction of CA (LM and LAD) with the presence of hemodynamically insignificant (HDIS) areas of stenosis (C) (CAD-RADs 2).

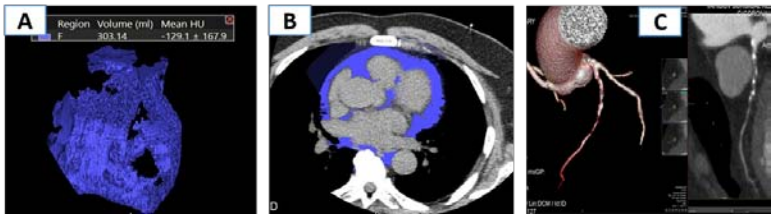


*Figure 8:* 65-year-old female patient. 3D-3D image of the EAT (A), axial projection with the designation of the EAT boundaries (B), curvilinear reconstruction of the CA with the presence of hemodynamically significant (HDS) areas of stenosis (C) (CAD-RADs 4).

Our results are consistent with the data of Bastarrika [3] and Damini Dey [7], who proved that patients with significant coronary artery stenosis had a slightly higher volume of EAT (154.58±58.91 cm3) in comparison with patients with HDIS coronary stenosis (120.94±81.85 $cm^3$, P=0.016).

In general, based on the analysis of similar foreign studies, it can be concluded that the threshold values of the EAT volume are equal to 125.14±56.88 $cm^3$, with the development of IHD, the EAT volume is 148.7 $cm^3$, and with significant coronary atherosclerosis - up to 299, 1 $cm^3$ [19]. According to the results of our study, with the development of ischemic heart disease, the volume of EFT was 169.6±56.2 $cm^3$.

According to Chumakovaet al., in evaluating the measurement data of the EAT thickness was taken as the threshold value of 6 mm, the EAT thickness ≥6 mm was a predictor of significant coronary atherosclerosis in patients with IHD [6]. It was also found that EAT thickness>7 mm in women is associated with subclinical coronary atherosclerosis [8]. According to our data, HDIS areas of stenosis were associated with an EAT thickness>7 mm. The high spatial resolution of the volumetric CT method makes it possible to study the direct effect of EAT on structural changes in the walls and atherosclerotic lesions of the coronary artery.

## V. Conclusion

Volumetric MSCT angiography of CA with the determination of EFT indicators allowed us to establish the presence of a correlation of varying degrees between the quantitative indicators of EAT (volume, thickness of EAT at the level of the interventricular septum, EAT area at the level of both ventricles) and the severity of coronary atherosclerosis.

The area of paracardial adipose tissue also correlates with the severity of coronary atherosclerosis,



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as the visceral fat depot has a systemic effect. As a result of the study, no relationship was found between the quantitative indicators of EAT and the age of patients.

The information obtained allows us to consider the change in the volume of EAT as an independent marker of the risk of developing CVD and can be used as a marker of the screening method in personalized diagnosis of coronary artery disease.

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*Conflict of Interests and Contribution of Authors*

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article and report on the contribution of each author.

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## References Références Referencias

1. Adam J. Nelson, MaddalenaArdissino and Peter J. Psaltis Current approach to the diagnosis of atherosclerotic coronary artery disease: more questions than answers. TherAdvChronicDis 2019, Vol. 10: 1–20.
2. Angela GallinaBertaso, Daniela Bertol, Bruce Bartholow Duncan, MuriloFoppa, Epicardial Fat: Definition, Measurements and Systematic Review of Main Outcomes. ArqBrasCardiol. 2013; 101(1): 18-28.
3. Bastarrika G, Broncano J, Schoepf UJ, et al. Relationship between coronary artery disease and epicardial adipose tissue quantification at cardiac CT: comparison between automatic volumetric measurement and manual bidimensional estimation. AcadRadiol2010; 17: 727–34.
4. Bettencourt N, Toschke AM, Leite D, et al. Epicardial adipose tissue is an independent predictor of coronary atherosclerotic burden. Int J Cardiol2012; 158: 26–32.
5. Bornachea O, Vea A, Llorente-Cortes V. Interplay between epicardial adipose tissue, metabolic and cardiovascular diseases. Clin.Investig.Arterioscler. 2018, 30, 230–239.
6. Chumakova G.A., Pokutnev A.P., Veselovskaya N.G., Bobrovskaya L.A. Relationship between the degree of epicardial fat volume and severity of coronary atherosclerosis. International Heart and Vascular Disease Journal Volume 6, Number 18, June 2018.
7. Damini Dey, Ajay Yerramasu, Shreenidhi Venuraju, et al. Increased volume of epicardial fat is an independent risk factor for accelerated progression of subclinical coronary atherosclerosis. Atherosclerosis J Elsevier 2012; 220(1): 223–30.
8. Ding J, Hsu FC, Harris TB, et al. The association of pericardial fat with incident coronary heart disease: the Multi-Ethnic Study of Atherosclerosis (MESA). Am J ClinNutr. 2009; 90: 499e504.
9. Glória Conceição, Diana Martins, Isabel M. Miranda, Adelino F. Leite-Moreira, RuiVitorino and InêsFalcão-Pires Unraveling the Role of Epicardial Adipose Tissue in Coronary Artery Disease: Partners in Crime? International Journal of Molecular Sciences. 23 October. 2020.
10. Gorter PM, De Vos AM, Graaf Y, et al. Relation of epicardial and pericoronary fat to coronary atherosclerosis and coronary artery calcium in patients undergoing coronary angiography. Am J Cardiol2013; 102: 380–5.
11. Ito T, Nasu K, Terashima M, et al. The impact of epicardial fat volume on coronary plaque vulnerability: insight from optical coherence tomography analysis. Eur Heart J Cardiovasc Imaging. 2012; 13: 408e415.
12. Neveen I. Samy, Mohammad Fakhry, Walaa Farid. Relation between Epicardial Adipose Tissue Thickness Assessed by Multidetector Computed Tomography and Significance of Coronary Artery Disease. World Journal of Cardiovascular Diseases, 2020, 10, 91-101.
13. Nerlekar N., Ha F.J., Cheshire C., et al. Computed tomographic coronary angiography-derived plaque characteristics predict major adverse cardiovascular events: A systematic review and meta-Analysis. CircCardiovasc Imaging 2018; 11:e00697.
14. Mahabadi AA, Massaro JM, Rosito GA, et al. Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study. Eur Heart J. 2009; 30:850e856.
15. Rosito GA, Massaro JM, Hoffmann U, Ruberg FL, Mahabadi AA, Vasan RS, et al. Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors, and vascular calcification in a community-based sample: the Framingham Heart Study. Circulation. 2008; 117(5):605-13.
16. Russo R, Di Iorio B., Di Lullo L, Russo D.Epicardial adipose tissue: New parameter for cardiovascular risk assessment in high risk populations. J. Nephrol. 2018, 31, 847–853.
17. Rishabh Khurana, Anurag Yadav T.B.S., Buxi J.P.S. Correlation of epicardial fat quantification with severity of coronary artery disease: A study in Indian population Indian Heart Journal 70 (2018) S140eS145.



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18. Rosito GA, Massaro JM, Hoffmann U, et al. Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors, and vascular calcification in a community-based sample: the Framingham Heart Study. Circulation. 2008; 117: 605e613.
19. Shehata S.M., F.M. Zaiton, M.H. Abo Warda. Role of MDCT in evaluation of epicardial fat volume as an independent risk factor for coronary atherosclerosis. The Egyptian Journal of Radiology and Nuclear Medicine 49 (2018) 329–337.
20. Dzhuraeva N.M. doctoral dissertation "Multivariate approaches to combined radiation and genotypic diagnosis of ischemic heart disease", Uzbekistan, Tashkent, 2018.



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# Global Journals Guidelines Handbook 2022

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# Memberships

## Fellows/Associates of Medical Research Council

### FMRC/AMRC Memberships

## Introduction

FMRC/AMRC is the most prestigious membership of Global Journals accredited by Open Association of Research Society, U.S.A (OARS). The credentials of Fellow and Associate designations signify that the researcher has gained the knowledge of the fundamental and high-level concepts, and is a subject matter expert, proficient in an expertise course covering the professional code of conduct, and follows recognized standards of practice. The credentials are designated only to the researchers, scientists, and professionals that have been selected by a rigorous process by our Editorial Board and Management Board.

Associates of FMRC/AMRC are scientists and researchers from around the world are working on projects/researches that have huge potentials. Members support Global Journals' mission to advance technology for humanity and the profession.

## FMRC

### Fellow of Medical Research Council

FELLOW OF MEDICAL RESEARCH COUNCIL is the most prestigious membership of Global Journals. It is an award and membership granted to individuals that the Open Association of Research Society judges to have made a 'substantial contribution to the improvement of computer science, technology, and electronics engineering.

The primary objective is to recognize the leaders in research and scientific fields of the current era with a global perspective and to create a channel between them and other researchers for better exposure and knowledge sharing. Members are most eminent scientists, engineers, and technologists from all across the world. Fellows are elected for life through a peer review process on the basis of excellence in the respective domain. There is no limit on the number of new nominations made in any year. Each year, the Open Association of Research Society elect up to 12 new Fellow Members.

## To the institution

### Get letter of appreciation

Global Journals sends a letter of appreciation of author to the Dean or CEO of the University or Company of which author is a part, signed by editor in chief or chief author.

## Exclusive Network

### Get access to a closed network

A FMRC member gets access to a closed network of Tier 1 researchers and scientists with direct communication channel through our website. Fellows can reach out to other members or researchers directly. They should also be open to reaching out by other.

Career | Credibility | Exclusive | Reputation


## Certificate

### Certificate, LoR and Laser-Momento

Fellows receive a printed copy of a certificate signed by our Chief Author that may be used for academic purposes and a personal recommendation letter to the dean of member's university.

Career | Credibility | Exclusive | Reputation


## Designation

### Get honored title of membership

Fellows can use the honored title of membership. The “FMRC” is an honored title which is accorded to a person’s name viz. Dr. John E. Hall, Ph.D., FMRC or William Walldroff, M.S., FMRC.

Career | Credibility | Exclusive | Reputation

## Recognition on the Platform

### Better visibility and citation

All the Fellow members of FMRC get a badge of "Leading Member of Global Journals" on the Research Community that distinguishes them from others. Additionally, the profile is also partially maintained by our team for better visibility and citation. All fellows get a dedicated page on the website with their biography.

Career | Credibility | Reputation

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## Future Work

### Get discounts on the future publications

Fellows receive discounts on the future publications with Global Journals up to 60%. Through our recommendation programs, members also receive discounts on publications made with OARS affiliated organizations.

Career | Financial

## GJ Internal Account

### Unlimited forward of Emails

Fellows get secure and fast GJ work emails with unlimited storage of emails that they may use them as their primary email. For example,
john [AT] globaljournals [DOT] org.

Career | Credibility | Reputation

## Premium Tools

### Access to all the premium tools

To take future researches to the zenith, fellows receive access to all the premium tools that Global Journals have to offer along with the partnership with some of the best marketing leading tools out there.

Financial

## Conferences & Events

### Organize seminar/conference

Fellows are authorized to organize symposium/seminar/conference on behalf of Global Journal Incorporation (USA). They can also participate in the same organized by another institution as representative of Global Journal. In both the cases, it is mandatory for him to discuss with us and obtain our consent. Additionally, they get free research conferences (and others) alerts.

Career | Credibility | Financial

## Early Invitations

### Early invitations to all the symposiums, seminars, conferences

All fellows receive the early invitations to all the symposiums, seminars, conferences and webinars hosted by Global Journals in their subject.

Exclusive

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## Publishing Articles & Books

### Earn 60% of sales proceeds

Fellows can publish articles (limited) without any fees. Also, they can earn up to 70% of sales proceeds from the sale of reference/review books/literature/publishing of research paper. The FMRC member can decide its price and we can help in making the right decision.

Exclusive | Financial

## Reviewers

### Get a remuneration of 15% of author fees

Fellow members are eligible to join as a paid peer reviewer at Global Journals Incorporation (USA) and can get a remuneration of 15% of author fees, taken from the author of a respective paper.

Financial

## Access to Editorial Board

### Become a member of the Editorial Board

Fellows and Associates may join as a member of the Editorial Board of Global Journals Incorporation (USA) after successful completion of three years as Fellow and as Peer Reviewer.

Career | Credibility | Exclusive | Reputation

## And Much More

### Get access to scientific museums and observatories across the globe

All members get access to 5 selected scientific museums and observatories across the globe. All researches published with Global Journals will be kept under deep archival facilities across regions for future protections and disaster recovery. They get 10 GB free secure cloud access for storing research files.

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## ASSOCIATE OF MEDICAL RESEARCH COUNCIL

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The primary objective is to recognize the leaders in research and scientific fields of the current era with a global perspective and to create a channel between them and other researchers for better exposure and knowledge sharing. Members are most eminent scientists, engineers, and technologists from all across the world. Associate membership can later be promoted to Fellow Membership. Associates are elected for life through a peer review process on the basis of excellence in the respective domain. There is no limit on the number of new nominations made in any year. Each year, the Open Association of Research Society elect up to 12 new Associate Members.

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A AMRC member gets access to a closed network of Tier 2 researchers and scientists with direct communication channel through our website. Associates can reach out to other members or researchers directly. They should also be open to reaching out by other.

Career | Credibility | Exclusive | Reputation


## Certificate

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Associates receive a printed copy of a certificate signed by our Chief Author that may be used for academic purposes and a personal recommendation letter to the dean of member's university.

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Career | Credibility | Reputation

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Financial

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Career | Credibility | Financial

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Exclusive


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Exclusive | Financial

## Reviewers

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Financial

## And Much More

### Get access to scientific museums and observatories across the globe

All members get access to 2 selected scientific museums and observatories across the globe. All researches published with Global Journals will be kept under deep archival facilities across regions for future protections and disaster recovery. They get 5 GB free secure cloud access for storing research files.

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| Associate | Fellow | Research Group | Basic |
|---|---|---|---|
| $4800<br>**lifetime designation** | $6800<br>**lifetime designation** | $12500.00<br>**organizational** | APC<br>**per article** |
| **Certificate,** LoR and Momento<br>**2** discounted publishing/year<br>**Gradation** of Research<br>**10** research contacts/day<br>**1 GB** Cloud Storage<br>**GJ** Community Access | **Certificate,** LoR and Momento<br>**Unlimited** discounted publishing/year<br>**Gradation** of Research<br>**Unlimited** research contacts/day<br>**5 GB** Cloud Storage<br>**Online Presense** Assistance<br>**GJ** Community Access | **Certificates,** LoRs and Momentos<br>**Unlimited** free publishing/year<br>**Gradation** of Research<br>**Unlimited** research contacts/day<br>**Unlimited** Cloud Storage<br>**Online Presense** Assistance<br>**GJ** Community Access | **GJ** Community Access |

# Preferred Author Guidelines

**We accept the manuscript submissions in any standard (generic) format.**

We typeset manuscripts using advanced typesetting tools like Adobe In Design, CorelDraw, TeXnicCenter, and TeXStudio. We usually recommend authors submit their research using any standard format they are comfortable with, and let Global Journals do the rest.

Alternatively, you can download our basic template from https://globaljournals.org/Template

Authors should submit their complete paper/article, including text illustrations, graphics, conclusions, artwork, and tables. Authors who are not able to submit manuscript using the form above can email the manuscript department at submit@globaljournals.org or get in touch with chiefeditor@globaljournals.org if they wish to send the abstract before submission.

## Before and during Submission

Authors must ensure the information provided during the submission of a paper is authentic. Please go through the following checklist before submitting:

1. Authors must go through the complete author guideline and understand and *agree to Global Journals' ethics and code of conduct,* along with author responsibilities.
2. Authors must accept the privacy policy, terms, and conditions of Global Journals.
3. Ensure corresponding author's email address and postal address are accurate and reachable.
4. Manuscript to be submitted must include keywords, an abstract, a paper title, co-author(s') names and details (email address, name, phone number, and institution), figures and illustrations in vector format including appropriate captions, tables, including titles and footnotes, a conclusion, results, acknowledgments and references.
5. Authors should submit paper in a ZIP archive if any supplementary files are required along with the paper.
6. Proper permissions must be acquired for the use of any copyrighted material.
7. Manuscript submitted *must not have been submitted or published elsewhere* and all authors must be aware of the submission.

**Declaration of Conflicts of Interest**

It is required for authors to declare all financial, institutional, and personal relationships with other individuals and organizations that could influence (bias) their research.

## Policy on Plagiarism

Plagiarism is not acceptable in Global Journals submissions at all.

Plagiarized content will not be considered for publication. We reserve the right to inform authors' institutions about plagiarism detected either before or after publication. If plagiarism is identified, we will follow COPE guidelines:

Authors are solely responsible for all the plagiarism that is found. The author must not fabricate, falsify or plagiarize existing research data. The following, if copied, will be considered plagiarism:

- Words (language)
- Ideas
- Findings
- Writings
- Diagrams
- Graphs
- Illustrations
- Lectures

- Printed material
- Graphic representations
- Computer programs
- Electronic material
- Any other original work

## Authorship Policies

Global Journals follows the definition of authorship set up by the Open Association of Research Society, USA. According to its guidelines, authorship criteria must be based on:

1. Substantial contributions to the conception and acquisition of data, analysis, and interpretation of findings.
2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

**Changes in Authorship**

The corresponding author should mention the name and complete details of all co-authors during submission and in manuscript. We support addition, rearrangement, manipulation, and deletions in authors list till the early view publication of the journal. We expect that corresponding author will notify all co-authors of submission. We follow COPE guidelines for changes in authorship.

**Copyright**

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**Appealing Decisions**

Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

**Acknowledgments**

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

**Declaration of funding sources**

Global Journals is in partnership with various universities, laboratories, and other institutions worldwide in the research domain. Authors are requested to disclose their source of funding during every stage of their research, such as making analysis, performing laboratory operations, computing data, and using institutional resources, from writing an article to its submission. This will also help authors to get reimbursements by requesting an open access publication letter from Global Journals and submitting to the respective funding source.

## Preparing your Manuscript

Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

***Manuscript Style Instruction (Optional)***

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

***Structure and Format of Manuscript***

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.

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## Format Structure

***It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.***

All manuscripts submitted to Global Journals should include:

**Title**

The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

**Author details**

The full postal address of any related author(s) must be specified.

**Abstract**

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

**Keywords**

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

**Numerical Methods**

Numerical methods used should be transparent and, where appropriate, supported by references.

**Abbreviations**

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

**Formulas and equations**

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

**Tables, Figures, and Figure Legends**

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.

**Figures**

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

## Preparation of Eletronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

## Tips for writing a good quality Medical Research Paper

***1. Choosing the topic:*** In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

***2. Think like evaluators:*** If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

***3. Ask your guides:*** If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

***4. Use of computer is recommended:*** As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

***5. Use the internet for help:*** An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.

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***6. Bookmarks are useful:*** When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

***7. Revise what you wrote:*** When you write anything, always read it, summarize it, and then finalize it.

***8. Make every effort:*** Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

***9. Produce good diagrams of your own:*** Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

***10. Use proper verb tense:*** Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

***11. Pick a good study spot:*** Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

***12. Know what you know:*** Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

***13. Use good grammar:*** Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

***14. Arrangement of information:*** Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

***15. Never start at the last minute:*** Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

***16. Multitasking in research is not good:*** Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

***17. Never copy others' work:*** Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

***18. Go to seminars:*** Attend seminars if the topic is relevant to your research area. Utilize all your resources.

***19. Refresh your mind after intervals:*** Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

***20. Think technically:*** Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

***21. Adding unnecessary information:*** Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

***22. Report concluded results:*** Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

***23. Upon conclusion:*** Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

## Informal Guidelines of Research Paper Writing

***Key points to remember:***

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

**Final points:**

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

*The introduction:* This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

**The discussion section:**

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

**General style:**

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

**To make a paper clear:** Adhere to recommended page limits.

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*Mistakes to avoid:*

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

**Title page:**

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

**Abstract:** This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

*Reason for writing the article—theory, overall issue, purpose.*

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

**Approach:**

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

**Introduction:**

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

*The following approach can create a valuable beginning:*

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

**Approach:**

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

**Procedures (methods and materials):**

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

**Materials:**

*Materials may be reported in part of a section or else they may be recognized along with your measures.*

**Methods:**

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

**Approach:**

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

**What to keep away from:**

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

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**Results:**

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

**Content:**

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

**What to stay away from:**

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

**Approach:**

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

**Figures and tables:**

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

**Discussion:**

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

**Approach:**

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

## The Administration Rules

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

*Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection*.

*Segment draft and final research paper:* You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

*Written material:* You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

## Criterion for Grading a Research Paper (Compilation) by Global Journals

**Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.**

| Topics | Grades | | |
|---|---|---|---|
| | **A-B** | **C-D** | **E-F** |
| ***Abstract*** | Clear and concise with appropriate content, Correct format. 200 words or below | Unclear summary and no specific data, Incorrect form Above 200 words | No specific data with ambiguous information<br>Above 250 words |
| ***Introduction*** | Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited | Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter | Out of place depth and content, hazy format |
| ***Methods and Procedures*** | Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads | Difficult to comprehend with embarrassed text, too much explanation but completed | Incorrect and unorganized structure with hazy meaning |
| ***Result*** | Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake | Complete and embarrassed text, difficult to comprehend | Irregular format with wrong facts and figures |
| ***Discussion*** | Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited | Wordy, unclear conclusion, spurious | Conclusion is not cited, unorganized, difficult to comprehend |
| ***References*** | Complete and correct format, well organized | Beside the point, Incomplete | Wrong format and structuring |

# INDEX


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