Editorial article

Evidence Based Medicine (EBM) -a short overview

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Abstract

Evidence based medicine (EBM) is the conscientious, explicit, judicious and reasonable use of up to date, best evidence in making decisions about the individual patient health care. EBM integrates clinical experience and patient values with the best available research information. It is an ideas which aims to increase the use of high quality clinical research in clinical decision making. EBM requires new skills of the health practitioner, including efficient literature-searching, and the application of formal rules of evidence in evaluating the clinical literature. When somebody wants to practice EBM he has to identify gaps in knowledge and formulate questions to fill those gaps, to conduct an efficient search in medical literature, to critically evaluate the research information and to apply this information to patient's care. EBM can minimize the errors in patient care, reduces the cost of treatment of the patient and optimizes the quality of patient care. The skills which has being learned when conducting EBM like those which were needed for being a lifelong, self- directed learner.

Key word: Evidence Based Medicine

Introduction:

Evidence-based medicine (EBM) is a systematic approach to clinical problem solving which allows the integration of the best available research evidence with clinical expertise and patient values.[1] This means relating individual clinical signs, individual clinical experience with the best scientific evidences obtained by the clinical research.[2] EBM deemphasizes (but not eliminate)intuition, unsystematic clinical experience and physiologic reasoning as sufficient grounds for clinical decision-making and emphasizes the systematic evaluation of evidence from clinical research.[3] EBM recognizes that the research literature is constantly changing .[4] What the evidence points to as the best method of practice today may change next month or next year. The primary aims of EBM were minimization of the using of non-documentary knowledge and reasoning in clinical practice and integration of clinical expertise, pathophysiologic knowledge and patient preferences in making decisions regarding the care of individual patients.[3]

History 0f EBM:

While some find traces of evidence-based medicine's origin in ancient Greece,[2,4] others trace its roots to ancient Chinese medicine.[5,6] Testing medical interventions for efficacy has occurred since the time of Avicenna's The Canon of Medicine in the 11th century[7,8] The concepts behind evidence -based practice has been increasingly accepted after the book of the Professor Archie Cochrane(a Scottish epidemiologist) Effectiveness and Efficiency: Random Reflections on health Services (1972). The EBM movement started in 1981 when a group of clinical epidemiologists at Mc Master University (Hamilton, Ontario, Canada), led by David Sackett, published the first of a series of articles in the Canadian Medical Association Journal advising physicians how to appraise the medical literature.[9,10] the term "evidence-based medicine" first appeared in the medical literature in 1992 in a paper by Guyatt et al[11], however, the founder of EBM is considered to be English epidemiologist

Archie Cochrane, who lived in the 19th century and which has already pointed out the impossibility of monitoring all the new discoveries in medical science [1].

Now EBM has been applied in management for every patient by doctors in western countries with the support of their governments, the ministries of health and pharmaceutical industry. This achieved by using practical guidelines for different diseases, a database with the best scientific evidence from each category, which is edited by special experts and which is continuously updated with new data, medical journals and literature available with the latest objective information.[10] when you have the EBM resources available in the hospitals, wards and clinic for immediate use, this is called point of care

Why we need EBM[3,11]?

There are many reasons leading to increase our interest in EBM. The most important ones were:

- Improves quality of patient care
- Standardize the delivery of healthcare
- Reduces the cost of health care
- Incorporates patients values into health care

For whom the EBM?

Not only for doctors,but for anyone involved in the health care system, including mangers and health planners.

How we can practice EBM?

A doctor or any health professional who wants to conduct EBM must able to understand the patient's circumstances or predicament (including issues such as social supports and financial Resources)he /she has to identify gaps in knowledge and formulate questions to fill those gaps, to conduct an efficient search in medical literature, to critically evaluate the research information and to apply this information to patient's care. This whole process has been divided into five simple steps, which if followed systematically can bring out a very successful outcome and a desired benefit to the patient care.[12]

The Five Steps EBM Model

5 As; Ask, Acquire, Appraise, Apply and Assess

Step1:*Ask*:Formulating answerable clinical questions

One of the difficult steps in practicing EBM to clinician is to translate the clinical problem into an answerable question.[13]

This means that clinician should develop the skills that enable them to convert the information which has been needed to answerable questions.

Good clinical questions should be clear, directly focused on the problem at hand, and answerable by searching the medical literature.[14] A good clinical question should have four essential components structured in the **PICO** format (**P**atient or problem, **I**ntervention, **C**omparison, **O**utcome).[1]

PICO format[1]:

- **P**atient or problem– who are the relevant patients, what kind of problem we try to solve?
- Intervention–what is the management strategy, diagnostic test or exposure (drugs, diagnostic test, foods or surgical procedure)?
- **C**omparison of interventions – what is the control or alternative management strategy, test or expo-sure that we will compare?
- **O**utcome – what are the patient-relevant consequences of the exposure in which we are interested?

In addition the clinician should add two other considerations when formulating their question.

Type of Question:

How would I categories this question? Is it related to etiology, diagnosis, therapy or prognosis?

Type of Study:

The other consideration is the type of study that will answer a formulate question. Various study designs provide specific answers (**table 1**).[3]

Example of PICO format:

In obese elderly patients with Type 2 Diabetes Mellitus (Problem),

is **Chlorpropamide** (Intervention) more efficient than **Metformin** (Comparison) in Controlling the blood glucose level (Outcome)?

Table 1: Type of study design to be selected for answering the question

Type of Question	Type of Study Design	Some words may be found in the title of the study
Therapy	Double-Blind Randomized Controlled Trial	Clinical Trials
Diagnosis	Controlled Trial	Sensitivity and Specificity or Diagnosis
Prognosis	Cohort Studies, Case Control, Case Series	Prognosis or Survival Analysis
Etiology	Cohort Studies	Risk factors
Prevention	Randomized Controlled Trial Cohort Studies	Prevention and Control

Step 2: *Acquire*: Finding the evidence

Once the clinician formulated his clinical question, the next step is to seek relevant evidence that will help him to answer his question. The aim effective searches are to maximize the potential of retrieving relevant articles within the shortest possible time[1]. The ideal information source is valid (contains high quality data), relevant (clinically applicable), comprehensive (has data on all benefits and harms of all possible interventions), and is user-friendly (is quick and easy to access and use).[1]

The basic search principles were Convert the clinical problem into an answerable question, Generate appropriate keywords, choose a bibliographic database and Conduct the search.[15]

Table (2): Type of research and its strength

Type of research methodology	Strength of the evidence
Double-Blind Randomized Controlled studies	Strong evidence 
Randomized Controlled studies	
Cohort studies	
Case control studies	
Case series	
Case reports	
Ideas , personal opinions	
Animal research	
In vitro (test tube) research	Weak evidence

When looking for articles on effectiveness of interventions or treatments, the first point of call should probably be the Cochrane database of systematic reviews or the other secondary sources such as Archimedes, Clinical Evidence, and Best Bets. The Cochrane controlled trials register provides an index of published randomized controlled trials.[15] MEDLINE is probably the most widely used database for searching the biomedical literature.[16] It is maintained by the National Library of Medicine, USA. A version of MEDLINE (PUBMED) is freely available on the internet, is updated regularly, and is relatively user friendly.[15]

Step 3: *Appraise*: Critical evaluation of the information

- Critical appraisal has been defined as the "application of rules of evidence to a study to assess the validity of the data, completeness of reporting, methods and procedures, conclusions, compliance with ethical standards, etc. The rules of evidence vary with circumstances.[17] Critical appraisal evolving looking for

research evidence in three main areas: Validity, importance, and applicability to the patient or patients of interest. Critical appraisal provides a structured but simple method for assessing research evidence in all three areas.[18] A structured approach to critical appraisal could potentially improve the quality of this process, and simple checklists can be useful to screen out research that is of low quality or of little relevance.[19]

- Did the study methods address the most important potential sources of bias?
- Was the study performed according to the original protocol?
- Does the study test a stated hypothesis?
- Were the statistical analyses performed correctly?
- Do the data justify the conclusions?

Are There were ten key questions can be used to assess the validity and relevance of a research article. These questions can assist clinicians to identify the most relevant, high-quality studies that are available to guide their clinical practice. [20]

- There any conflicts of interest?

Clinician can develop critical appraisal skills which involve learning how to ask a few key questions about the validity of the evidence and its relevance to a particular patient or group of patients through small tutorials, workshops, interactive lectures, and at the bedside teatching.[18] Several tools for appraising research articles are available; one of it is the Critical Appraisal Skills Programme (CASP), Oxford, UK, which include tools for appraising randomised controlled trials, systematic reviews, case–control studies, and cohort studies. The CASP tools are simple, easy to use, and freely available on the internet.[21]

Step4. *Apply*: Application of information of the patient:

Application of gained information on the special circumstances pertaining to each patient is the crucial and the most complex step in Evidence Based Medicine. There were questions that we should ask before we decide to apply the results of the study[1]**:**

Step 5. *Assess*: Evaluating the Process:

Ten questions to ask when critically appraising a research article.

- Is the study question relevant?
- Does the study add anything new?
- What type of research question is being asked?
- Was the study design appropriate for the research question?
- Do the potential side effects of the drug or procedure outweigh the benefits?
- Are the outcomes appropriate to the patient?
- Does the treatment conflict with the patient's values and expectations?
- If something does not exist, it is necessary to weigh the potential harm from the benefit and do all that in partnership with the patient.
- Is the treatment available and is health care system prepared to fund it?
- What alternatives are available? Are the participants in the study similar enough to my patient?

As the clinicians use the EBM into their routine clinical practice, they need to evaluate their approach time to time to decide whether they need to improve on any of the four steps discussed above. The clinicians need to ask whether they formulating answerable questions, finding good evidence quickly, effectively appraising the evidence, and integrating clinical expertise and patient's values with the evidence in a way that leads to a rational, acceptable management strategy. [22]The clinicians should document the outcomes of the application of the evidence and present it to their colleagues in formal audit and they should be able to develop management consensus. After that they must collaborate with medical scientific societies and professional bodies in developing practice guidelines. The last step leads to completion of the feedback loop of the EBM.

Limitations of Evidence Based Medicine:

There are many challenges or limitations in adopting EBM like[3]:

- The availability of the technology and online information to the clinician.
- Lacking of clinician's skills which required for accessing the medical literature and finding the best evidence.
- Lacking of moral, ethical, and professional obligation of providing the current best health care to the patients.
- Publication bias and major deficiencies in the design, analysis and reporting of the research findings.
- Over-reliance on statistical significance of the evidence as opposed to clinical significance.

Conclusion:

EBM can improve the quality of care when there is integration of best research evidence with clinical experience and patient's preferences, so EBM can minimize the errors in patient care, reduces the cost of treatment of the patient and optimizes the quality of patient care. EBM requires from clinician new knowledge, access to medical database, the ability to search medical literature and basic skills in interpretation of epidemiological and statistical results. The skills which have being learned when conducting EBM like those which were needed for being a lifelong, self- directed learner.

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Abstract

Background: As approved by many studies patients with H. pylori infection; a spiral bacterium that invade different parts of gastrointestinal tract and mainly gastric mucosa causing gastric inflammation and peptic ulceration may linked directly to body iron status.
This study aimed to evaluate the body iron status in H .pylori infected patients
Methods: This study was conducted in Kosti Teaching Hospital, White Nile State (Sudan) Jan 2018 to March 2019. The study groups consisted of 58 patients with H. pylori as cases group and another group were 58 healthy subjects as the control group. The members of both groups were enrolled in the study voluntarily. Study groups demographic and anthropometric data, hemoglobin, serum ferritin and total iron- binding capacity and transferrin were measured.
Results: Hemoglobin, serum ferritin (11.32 vs. 79.15 ng/ml) was significantly lower when compared with the control one. On other hand transferrin and total iron-binding capacity statistically reflected higher figures as (397.05 vs. 265.11 mg/dl) and (543.21 vs.270.42 mcg/dl) respectively when compared case group with control one. Moreover endoscopy screening of patients reflected considerable information regarding esophagitis, gastritis, duodenal ulcer and esophageal cancer.
Conclusion: Although the findings of present study revealed that H. pylori are able to interfere with the distribution of biological iron, reflecting significant alteration on parameters related to iron homeostasis. Since evidence for the association of H. pylori and IDA still not enough and there are contrasting data about such association, future high quality and cohort researches are needed to determine the causal association.

Keywords: H. pylori, Transferrin, Total iron-binding capacity, Ferritin.

Introduction:

The distribution of iron in human body is regulated at different levels including the intestinal absorption, contribution of iron in body activities, hepatic storage and export process. Many proteins play major roles in regulation, homeostasis and maintenance of iron status. The most known proteins are ferritin, transferrin, and total iron binding protein, transferrin receptor, ferroprotein and hepcidin. Transcriptions of all this proteins approved to be regulated at the modification level that involve the post transcribed messenger RNA by stored fraction, and considerable effect on the process of transcription by hormones, inflammatory reaction beside hypoxia.[1] Infection with H. pylori was associated with a reduced level of biological iron pool that seems to be attributed to the cellular response of the infected host to the bacterial components. Clinically reduction in the level of serum iron would be reflected as reduction in hemoglobin and serum ferritin beside increased in the amount of total iron binding capacity (TIBC) and transferrin.[2]

Iron deficiency anemia is the most common cause of anemia in the world. Anemia defined as a reduction in the number of red blood cells (RBCs) or the amount of hemoglobin (Hb) concentration below established standard levels. Based on the World Health Organization reports almost a quarter of the world population is anemic.[3]

The main causes in children are the shortage or lack dietary iron while in adult males is almost result from chronic blood loss due to gastrointestinal bleeding and menstrual bleeding in women.[4,5] Most significant laboratory finding including lowering in mean cell volume (MCV), mean cell hemoglobin concentration (MCHC),levels of serum ferritin, increased total iron binding capacity(TIBC).

In peripheral blood of patients the predominant is hypochromic microcytic red blood cell (RBC). [6] Various recent studies that said the underlying causes of anemia are chronic gastritis associated with Helicobacter pylori infection, peptic ulcer and gastric carcinoma. Various studies are suggesting that H. pylori infection as a risk factor for iron deficiency anemia.

Many studies related the mechanisms to reduction in the secretion of Hydrochloric acid (HCL).[7,8] H. Pylori infection is the most common cause of gastritis in Sudan. [9] Another studies suggested an association between H. pylori infection and iron deficiency anemia. [10, 11]

Objectives:

To study the effect of H. pylori infection on iron profile

Materials and Methods:

Approval permission of this study was received from the administration of Kosti Teaching Hospital, White Nile State, Sudan Routine verbal consents for laboratory diagnosis were implemented for all subjects according to hospital regulations and the study protocol conformed to the ethical guidelines of research in the state. The study was conducted in white Nile State, Sudan,enrolled 116 human subjects divided into two groups; H. pylori-positive Case group (n=58) was defined by positive documentation of at least two of the three laboratory test results (H.pylori stool antigen, selective culturing, ICT serological test), and H. pylori-negative (Control) group (n=58) with negative laboratory tests for H. pylori. Clinical histories for all participants for the present of gastro-intestinal symptoms including recurrent Abdominal Pain (RAP), recurrent vomiting and chronic anorexia for three months were taken, beside that weight and height of study groups were measured and recorded in this study.

Patients with hematologic disorders (e.g. sickle cell anemia), immunological or metabolic disorders, food allergy (celiac disease), collagen vascular diseases or children receiving antibiotics for last four weeks or receiving antisecretory therapy for last two weeks, as well as patients with past or family history of psychic element were all excluded from this study. All cases were matched with eligible control group for age, sex, education and other socio-demographic variables to rule out any possible confounders.

Detection of H. pylori Infection.

H.pylori infection was laboratory diagnosed via H. pylori stool antigen test, selective culture for gastric aspirate as well as detection of anti-H. Pylori antibodies (ICT).Then positively tested patients underwent esophagogastroduodenoscopy (OGD)

Estimation of Hemoglobin, Ferritin, transferrin and total iron binding capacity

5ml blood taken from all participates. 2ml was used to determine the level of hemoglobin while the reminder processed to obtain the needed serum for estimation of ferritin, transferrin and total iron binding capacity using commercial diagnostic kits and carefully following the enclosed instructions.

Statistical Analysis:

Data collected, organized, and processed tabulated and analyzed. A confidence interval with 95% was calculated. Data analyses in the current study were performed through SPSS, version 18.0 (SPSS Inc., Armonk, NY, USA).

Results:

General characteristics Of 116 subjects that referred to laboratory of Kosti Teaching Hospital, 67% of them were females and 33% were males. The mean age of cases

was 26.21 ± 7.9 while that of control group was 29.15±6.5.

Endoscopy screening of patients

Esophagogastroduodenoscopy (OGD) findings in case group reflected the presence of esophagitis, gastritis, duodenal ulcer and cancer of esophagus among this group while no evident of gastric tumor, **Table (1)**.

Table 1: Esophagogastroduodenoscopy(OGD) Findings in Case Group

OGD Finding	No of Patients	Percent (%)No = 58
Esophagitis,	4	6.89%
Gasteritis	20	34.48%
Duodenal Ulcer	9	15.52%
Cancer of Esophagus	2	3.45%

Hemoglobin, Ferritin, transferrin and TIBC Levels.

Among the cases group the mean level of hemoglobin was 7.94 ±0.6 mg/dl while that of control group was14.34±0.9 mg/dl. Serum ferritin levels is 11.32 ±4.5 (ng/ml) in case group while that of control group was 79 ±6.8 (ng/ml). TIBC and transferrin showed an increased levels in case group 543 vs. 270 mcg/dl and 397 vs. 265 mg/dl respectively, **Table (2)**.

Table 2: The distribution of Hb ,Ferritin,Transferrin & TIBC levels among study groups

Group	Hb (mg/dl)	Ferritin(ng/ml)	TIBC (mcg/dl)	Transferrin(mg/dl)
Patients	7.94 ±0.6	11.32±4.5	543.21 ±34.12	397.05± 43.35
Controls	14.34±0.9	79.15±6.8	270.42±28.32	265.11±45.27

Discussion:

The current topic revealed strong association between reductions in the level of hemoglobin among H. pylori infected subjects when compared with H. pylori free group. These findings were supported with the study published regarding the association between H. pylori infection and anemia due to iron deficiency in 1991.[12] later on much research conducted and approved this association. For example a case report study concerning 14 cases revealed clear association between H. Pylori infection and ID or IDA among children.[13,14] Iron deficiency anemia (IDA) patients with H. pylori infection who received H.pylori treatment had a significantly greater increases hemoglobin level one month following H. pylori treatment compared to IDA patients with H. pylori infection who did not receive H. pylori treatment.[14] Multiples studies focusing on the epidemiology of the H. pylori infection reported findings of association between the bacteria and occurrence of iron deficiency and iron deficiency anemia (ID/IDA) in both developed and developing countries.[14,15] Eradication of H. pylori for refractory IDA is supported by most of the current evidences. However, larger sample and well-constructed study design are necessary to clarify the association between H. pylori infection, iron deficiency and iron deficiency anemia.[16,17] Low ferritin level observed in our study (Table 2) is matching that shown by epidemiological studies involved persons seropositive for H. pylori infection seem to have a significantly lower serum ferritin level.[18]In a population- based study(n=2794) from Denmark, H. pylori - seropositive persons were at 40% increased risk of having reduced serum ferritin level (<30µg/L) compared to seronegative individuals(after adjustment of age, gender, menopausal status, socioeconomic status, blood donation, and alcohol consumption) .[19] The effect of the bacteria on the metabolism of iron approved in studies conducted by Milman et al.[19] and

Seo et al. their studies showed reduction in serum ferritin levels in children with H. pylori infection. Other studies searched more deep in this direction linking H. pylori infection with iron deficiency. In study regarding iron profile the output showed an increased in the level of transferrin and total iron binding capacity in patients than in healthy group. The effect of H. pylori on iron level can be reflected on proteins that involve in iron metabolism. A study of Alaskan natives (n=2080) found increased risk of low serum ferritin in persons seropositive for H. pylori infection. Berg et al[18] in their study have shown that H. pylori infection cause decrease in serum ferritin level that consistent with our results.

The report by Epidemiologic studies also support an association between H. pylori infection and low iron stores, and several reports have shown resolution of refractory cases of anemia after H. pylori treatment.[20] Also Choe et al. have shown that H. pylori result in IDA with decreased level of hemoglobin and ferritin and increased level of transferring and TIBC.[21] The mechanism by which H. pylori gastritis could cause iron deficiency anemia still need advanced researches. Although several mechanisms have been taken as hypothetical explanation regarding the possible effect of H. pylori infection on iron stores many of them approved that blood lost during the gastrointestinal bleeding accompanied with H. pylori infection is not the likely the main causes. Since most published studies found no bleeding lesions in those cases diagnosed as iron deficiency anemic patients and investigation of the subjects showed negative fecal occult blood testing.[21-23]

The most accepted mechanism is the effect of the bacteria on the absorption of iron due to hypo-or achlorhydria result from gastritis that associated with the infection. Gastric hydrochloric acid facilitates iron absorption by reducing non-heme iron from the ferric to ferrous form.[19] Persons with H. pylori infection and IDA appear more likely to have corpus gastritis as compared to H. pylori-infected patients without anemia.[24,20] Corpus gastritis results in decreased gastric acid secretion and increase in intragastric pH that may impair iron absorption.[19] Acid secretion returns to the normal range after eradication of H. pylori.[21] Another possible mechanism by which H. pylori could result in decreased availability of iron is sequestration of iron in lactoferrin in the gastric mucosa. H. pylori takes up iron from human lactoferrin through a receptor-mediated method,[25,26] and lactoferrin secretion in the gastric mucosa appears to be influenced by the H. pylori organism. [21] Since gastric mucosa lactoferrin levels have been shown to be significantly higher in H. pylori-positive IDA persons compared to persons who are non-anemic H. pylori-negative, nonanemic H. pylori-positive and H. pylori-negative with IDA.[21]

The other effect of H. pylori gastritis that may cause reduced iron absorption is a decrease in the concentration of ascorbic acid in gastric secretion. The vitamin; ascorbic enhance iron absorption by reducing iron to the ferrous form.[27]

Ascorbic acid is secreted into gastric juice, and it has been shown that gastric juice ascorbic acid levels are significantly lower in H.pylori-infected vs. uninfected persons, [24] and those ascorbic acid level increases after cure of H. pylori infection. [25]

Conclusion:

The current study reflected significant association between H. pylori infection and iron status in the body that reflected as reduction in hemoglobin and ferritin while TIBC and transferring were elevated.

Recommendation:

Patients with iron deficiency anemia (IDA) should be screened for H. pylori infection and much effort need to be done for to clarify the association between iron deficiency anemia and H. pylori infection.

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Original Articles

Prevalence of Non-alcoholic Fatty liver Disease in patients of Diabetes Mellitus in Referred Clinic in Kosti Teaching Hospital, Kosti city, White Nile State, Sudan

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Abstract

Introduction:
Non-alcoholic fatty liver disease (NAFLD) is very common pathological conditions worldwide that is closely associated with the clinical features of metabolic syndrome and is characterized by substantial inter patient variability in severity and rate of liver disease progression.
Methods:
This is a prospective hospital based study which was performed in Kosti city-White Nile State (Sudan). The study population comprised diabetic patients whom are randomly selected from Kosti Teaching Hospital. It was conducted in the period between 1/2/2019 to 1/4/2019.The sample size was on an average of 150 cases, categorized further into 80 cases and 70 controls. All cases were subjected to full history, proper examination, lab investigations and abdominal ultrasound. Information were collected, classified into three forms of data and analyzed accordingly.
Results:
The overall prevalence of non alcoholic liver disease in diabetes mellitus is 68%. This prevalence increases with age as there is remarkable increase in developing nonalcoholic liver disease mainly in patients of old ages. The prevalence has gender variation as it reveals predominance of female in diabetes and diabetes with hypertension and no gender variation in diabetes with coronary artery disease. Prevalence of non alcoholic liver disease increased in urban areas in diabetes with coronary artery disease and increased in rural areas in diabetes and diabetes with hypertensive patients. Prevalence of nonalcoholic liver disease increased with duration of diabetes mellitus.
Conclusion:
Based on the findings of the presents study, the prevalence of nonalcoholic fatty liver disease in diabetes mellitus is related to age, sex, residence, duration of disease.

Key words: nonalcoholic fatty liver disease (NAFLD), diabetes mellitus (DM), hypertension (HTN), coronary artery disease (CAD).

Introduction:

Nonalcoholic fatty liver disease (NAFLD) represents a spectrum of progressive liver disease occurring in the absence of excessive alcohol consumption that ranges from isolated intra hepatic triglyceride accumulation (simple steatosis), through intra hepatic triglyceride accumulation plus inflammation and hepatocyte injury (non-alcoholic steatohepatitis, NASH), and ultimately progresses to fibrosis /cirrhosis and potentially hepatocellular carcinoma. Although a significant proportion of the population has NAFLD, only a minority progresses to advanced liver disease or liver-related death.[1] Epidemiological studies indicate that type 2 diabetes mellitus and concomitant hypertension are associated with high risks of macrovascular and microvascular complications as well as clinical adverse cardiovascular accident.[2]
Although the factors such as excessive caloric intake and insulin resistance are involved in pathogenesis of hypertension in type 2 diabetes mellitus and these have been targeted for therapeutic intervention, however, up to now, the mechanisms facilitating hypertension in type2 diabetes

mellitus individuals are still not very clear. More research studies are needed to determine the causes of hypertension in type2 diabetes mellitus.[2]

Nonalcoholic fatty liver disease (NAFLD) has been increasing worldwide in the last decades and is occurring in up to 75% among patients with type 2 Diabetes mellitus(DM). [3] It has been suggested that NAFLD could increase the risk of insulin resistance (IR) and may be involved in the pathogenesis of cardiovascular disease in type2 diabetes mellitus (DM) .[4] However, currently, there has been scarce literature on the study of high metabolic risk of hypertension in type 2 diabetes mellitus with or without NAFLD.

Little is known about the relationship between NAFLD and hypertension in this patient population, which limits the understanding of the relative crosstalk between NAFLD and the other metabolic risks contributing to prevalent hypertension in type2 diabetes mellitus. Taking into account that NAFLD is the most common chronic liver disease among patients with type2 diabetes mellitus, studying the effects of NAFLD on the pathogenesis of hypertension should be considered in type2 diabetes mellitus with and without NAFLD separately.[5 -7] In prashnath et al study, 87% had NAFLD on histology with 62.6% steatohepatitis and 37.3% fibrosis.[6] Age, duration of diabetes mellitus, degree of glycemic control, body mass index, waist circumference, family history of diabetes mellitus, did not predict the presence or severity of NAFLD or fibrosis[6]. Serum alanine aminostranferase (ALT) and alkaline phosphatase levels, though within normal limits, were significantly higher in patients with steatohepatitis. Prevalence of nonalcoholic steatohepatitis (NASH) increased with increase in the components of the metabolic syndrome. Serum AST / ALT ratio were also significantly higher in patients with severe fibrosis.[6,8]

Justification:

This study was undertaken for a variety of reasons:

- The high incidence of diabetic patients in target area.
- Despite of its importance, the prevalence of NAFLD among diabetic patients is not well reviewed, not only in White Nile State, but also in whole Sudan.
- The relevance and national importance of the target area (Kosti city).
- Establish a database and a reference through which further study can be undertaken.

***Aim of the study*:**

To know the prevalence of nonalcoholic fatty liver disease in diabetic patients and its relation to age, sex, residence and duration of the disease.

Materials and Methods:

This is a prospective hospital based study. The study was performed in Kosti city-White Nile State. The study population comprises diabetics (32 patients), diabetes associated with hypertension (32 patients) and diabetes with coronary artery disease(16 patients). Patients were randomly selected from medical referred clinic of Kosti Teaching Hospital. The study was conducted in the period between, 1/2/2019 and 1/4/2019.

Study population:

The study included 150 patients diagnosed with diabetes, diabetes with hypertension and diabetes with coronary heart disease as a group from which the cases were selected. The patients were randomly selected from medical referred clinic of Kosti Teaching Hospital**.** The inclusion criteria for the study population were patients with type 2 diabetes, diabetes associated with hypertension and diabetes with coronary artery disease patients on treatments. All patients above 50 years of age with disease duration of 10 years and above.

Data collection:

A brief description for the aim of the study was explained to the patients, and verbal consent was obtained. The data was collected through data forms of 3 types -

Data form 1→ contains the following: Personal information of the patients, name, age, sex, marital status, tribe, residence, housing condition , brief history of his illness, duration, disease control, other co morbidities, treatment; brief examinations and recent finding if there; Data form 2→ include the following investigations random blood (RBG), aspartate aminotransferase (AST) and alanin aminotransferase(ALT), urine analysis and glycosylated hemoglobin (HbA1c). Data form 3→ contains the findings in abdominal ultrasonography. Abdomenal ultrasonography was used for the detection and gradation of NAFLD according to the standard criteria accepted by the American Gastroenterology Association.[9]

Statistical method:

All relevant statistics were performed using the Statistical package for social sciences (SPSS Ver-20.0, SPSS) software. The mean and standard deviation (SD) of all parameters were expressed. Analysis of variance(ANOVA) was used for comparison of mean between the groups. The relationship between the parameters were obtained by Pearson's correlation matrix (r) and a value of $P< 0.05$ was considered (at 95% CI) to be statistically significant

Ethical certificate:

The ethical approval for this research was obtained from the ethical committee of Ministry of Health- White Nile State before conduction of this research.

Results:

The overall prevalence of NAFLD in diabetes mellitus is 68 %(54 patients out of 80 patients).The overall prevalence of NAFLD in diabetes is 43 % (14 patients out of 32patients), in diabetes with hypertension is 75%(24 patients out of 32 patients) and diabetes with coronary artery disease is 100%(16 patients out of 16 patients) . (**figure1**)

The prevalence of NAFLD is 26% in Diabetes (14 patients out of 54 patients), 44% in diabetes with hypertension (24 patients out of 54patients) and 30% of diabetes with coronary artery disease (16 patients out of 54 patients).

The prevalence of NAFLD in diabetes increases with age, as there is remarkable increase in developing NAFLD mainly in patients of old ages. (**Table1**)

The prevalence of NAFLD in diabetes mellitus has gender variation as it reveals high predominance of female in diabetes, mild predominance of female in diabetes with hypertension and no gender variation in diabetes with coronary artery disease (**Table 2**).

Prevalence of NAFLD increased in urban areas in diabetes with coronary artery disease and increased in rural areas in diabetes and diabetes with hypertension (**Table 3**).

Prevalence of NAFLD increased with duration of diabetes as higher prevalence noticed with longer duration of diabetes (**Table 4**).

Table 1 : Prevalence of NAFLD in DM related to age categories.

	Diabetes		**DM+ HTN**		**DM+ CAD**	
Age group	No(14)	prevalence %	No(24)	prevalence %	No(16)	prevalence%
50-59 years	3	21.5%	5	20.9%	0	0%
60-69 years	5	35.7%	7	29.1%	3	18.7%
70-80 years	6	42.8%	12	50%	13	81.3%
Total	14	100%	24	100%	16	100%

Table 2 : Prevalence of NAFLD in DM according to gender variation

Gender	Diabetes No(14) prevalence %	DM+HTN No(24) prevalence%	DM+CAD No(16) prevalence%
Male	3 21.4%	11 45.8%	8 50%
Female	11 78.6%	13 54.2%	8 50%
total	14 100%	24 100%	16 100%

Table 3: Prevalence of NAFLD in DM according to Residency

Residence	Diabetes No(14) prevalence %	DM+HTN No(24) prevalence %	DM+CAD No(16) prevalence%
Urban	5 35.7%	9 37.5%	12 75%
Rural	9 64.3%	15 62.5%	4 25%
total	14 100%	24 100%	16 100%

Table4: Prevalence of NAFLD in DM according to duration of disease

Duration of disease	DM No(14) prevalence %	DM+HTN No(24) prevalence%	DM+CA No (16) prevalence%
10-15 yrs	6 42.1%	3 12.5%	0 0%
16-20 yrs	8 57.9%	6 25%	1 6.3%
>20 yrs	0 0%	15 62.5%	15 93.7%
Total	14 100%	24 100%	16 100%

Table 5: Means and standard deviations of main parameters in the prevalence of NAFLD in DM

Cases categories:	Parameters RBG	AST	ALT	P value
DM	201.+/-100.7	29.3+/-9.2	31.2+/-8.7	0.02*
DM with HTN	211.2+/-94.2	31.9+/-11.6	32.4+/-10.6	0.01*
DM with CAD	302.4+/-74.2	41.9+/-10.9	39.0+/-9.6	0.013*

* P value < 0.05 indicates significant differences
**P value > 0.05 indicates no significant differences

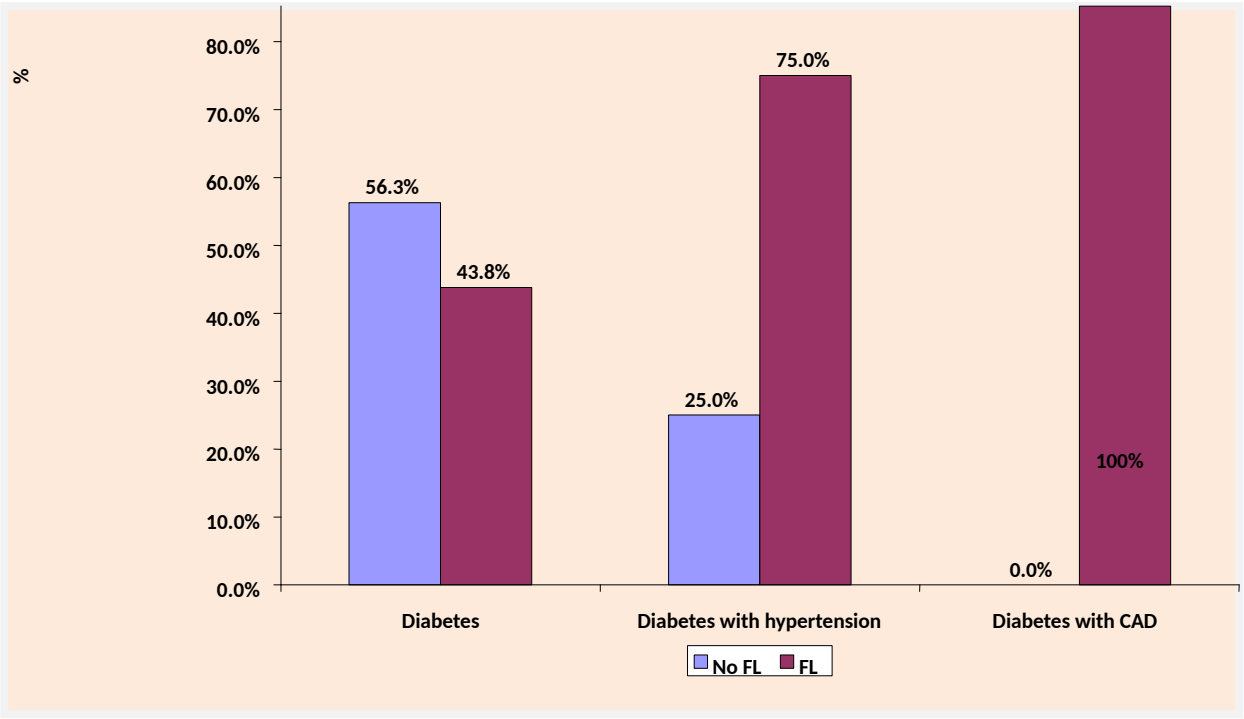

Figure 1: The overall prevalence of NAFLD in diabetes, diabetes with hypertension and diabetes with coronary artery disease using ultrasound.

Discussion:

Our study evaluated 150 patients diagnosed with diabetes, diabetes with hypertension and diabetes with coronary heart disease. The prevalence of NAFLD in the three categories is related to the age of the patients. The age categories were 50-59 years,60-69 years and 70-80 years with prevalence21.5%,35.7%,42.8% respectively in diabetes, 20.9%, 29.1% ,50% respectively in diabetes with hypertension, 0%, 18.7%, 81.3%respectively,in diabetes with coronary artery disease (**Table1**).

There is remarkable increase in developing NAFLD mainly in patients of old ages Comparable to Prashanth et al[6] determined the prevalence and risk factors of NAFLD among Indian patients with diabetes mellitus.

The prevalence of NAFLD in males reveals 21.4% in diabetes, 45.8% in diabetes with hypertension, 50% in diabetes with coronary artery disease and in females 78.6%, 54.2% and 50% respectively(**Table2**). This in line with the findings of Summart U et al[10], in a total of 34,709 participants (27,073 females and 7,636 males). They found that the prevalence of NAFLD in women was 22.9% whereas it was only 18.3%.

The prevalence of NAFLD in diabetes among urban areas reveals 35.7% in diabetes,37.5% in diabetes with hypertension ,75% in diabetes with coronary artery disease, possibly due to sedentary life style, smoking and westernized food while in rural areas reveals 64.3% in diabetes, 62.5% in diabetes with hypertension, 25% in diabetes with coronary artery disease possibly due to lack of health awareness, noncompliance and the bad storage of treatment (**Table3**).

On the contrary to the recent findings of Davendra K. et al (2019)[7] who found that prevalence of NAFLD was higher in urban patients (58.75%) than the rural patients (31.25%).

The prevalence of NAFLD also related to duration of disease as it reveals in diabetes 42.9%, 57.1%, 0% in the duration of 10-15 years,16-20years and>20 years respectively. In diabetes with hypertension it reveals

12.5%, 25%, 62.5% in the duration of 10-15years, 16-20 years and >20 years respectively. In diabetes with coronary artery disease it reveals 0%, 6.3%, 93.7% in the duration of 10-15 years, 16-20 years and >20 years respectively (**Table4**). The overall prevalence of NAFLD in diabetes, diabetes with hypertension and diabetes with coronary artery disease through using ultrasound machine constitutes 43.**8%**, 75%and 100% respectively (Figure1).This is in agreement with the study carried by Baharvand-A. et al (2016) which studied the prevalence of NAFLD in patients with coronary artery disease among Iranian subjects.[11] They found significant difference between patients with NAFLD associated with coronary artery disease and those with NAFLD without coronary artery disease.

***Conclusion*:**

Based on the finding of this study, the overall prevalence of NAFLD in diabetes mellitus is 68%. This prevalence increases with age as there is remarkable increase in developing NAFLD mainly in patients of old ages. The NAFLD is predominant in female with diabetes and diabetes with hypertension but has no gender variation in diabetic patients with coronary artery disease. Prevalence of NAFLD increased with the duration of diabetes mellitus. Prevalence of NAFLD increased in urban areas in diabetes with coronary artery disease and increased in rural areas in diabetes and diabetes with hypertension.

Recommendations:

- Establish a center of liver disease in Kosti Teaching Hospital not only for NAFLD but also for other liver diseases.
- Introduction of abdominal ultrasonography as a routine tool in follow up of diabetic patient to detect early stages of NAFLD.
- Establishment of a dietitian center in Kosti Teaching Hospital to orient patients for using healthy food and maintaining optimum weight.
- Patients of DM with HTN and DM with CAD should be followed up using all liver profile in every visit.
- Further study of NAFLD including large number of samples is needed.

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Original Articles

Prevalence of *Schistosomia haematobium* and Associated Risk Factors Among School Children in Algablin village, White Nile State, Sudan.

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Abstract

Background: Schistosomiasis is a water parasitic disease infecting more than 200 million people, it is the third after malaria and intestinal helminthiasis in global parasitism. The negative impacts on school performance and the debilitation caused by untreated infections demoralize both social and economic development in endemic areas.

Aim: To determine the prevalence of urinary schistosomiasis among basic school children in Algablin village.

Methods: This cross sectional study was carried out from May to July 2018 in Algablin village, White Nile State. Sudan, . Two hundred urine samples were collected from school children in Algablin village and examined for the parasite using parasitological filtration concentration techniques.

Results: Out of 200 urine samples examined, the prevalence of *S.haematobium* was 24%. In Abo Bakr Alsedig School the prevalence of urinary schistosomiasis was 25% and in Khalid Ibn Al Walid school the prevalence of infection was 23%. Regarding to the age groups, in the group (8-10) years, the prevalence of the disease was 26%, and in age (10-13) years the prevalence of infection was 22%.

Conclusions: The study concluded that the prevalence of *S.haematobium* parasite infection is 24% in the studied area, and that the prevalence of urinary schistosomiasis was higher in age group 8-10 years than age group 11-13years.

Keywords: Prevalence; Schistosomiasis; *S.haematobium*. risk factors; Filtration Technique.

Introduction:

Schistosomiasis (Bilharzia) known as snail fever, it is water born parasitic disease caused by Schistosoma[1], it is the digenic treamatode found in the blood vessels of man. The negative impacts of the disease on school performance and the debilitation caused by untreated infections demoralize both social and economic development in endemic areas.[2] Most common infections are caused by *S. haematobium, S. mansoni, and S. japonicum*, less prevalent species include *S. mekeongi* and *S. intercalatum*. Schistosomiasis is endemic in tropical and subtropical areas it is the major cause of morbidity and mortality; estimates of infected individuals worldwide are 237 million and another 600–779 are at risk of being infected.[3] Urogenital schistosomiasis, caused by *S. haematobium,* is characterized by hematuria, dysuria, bladder wall pathology, hydronephrosis, and it can also lead to squamous cell carcinoma.[2,4] In adults, the infection can cause genital ulcers and other lesions [5], Resulting in poor reproductive health, with sexual dysfunction and infertility [6] The prevalence rises rapidly from the age when young children begin to wander field. The peak prevalence and intensity of infection occur in children aged (10-14) years.[7,8] Studies also suggest that HIV/AIDS is highly prevalent in the areas of parasitic worm infections, such as schistosomiasis.[9-12]

Since the sources of water supplies in majority of rural areas in White Nile State are canals, few latrines, and lack of fresh water; Contaminated water is use for

washing clothes, agricultural purposes, fishing and swimming leading to increased rate of schistosomiasis.[13-15] therefore, the present study was aimed to measure the prevalence of urinary schistosomiasis among school children according to the age groups.

Materials and Methods:

Study design:

This cross-sectional descriptive study was conducted in White Nile State, Algablin village, Sudan during May to July 2018. Two schools were selected, Abo Bakr Alsedig (far away from the river) and Khalid Ibn Al Walid (nearby). The main character of the area is location near to the river.

Study population

A total 1500 School children aged from 9-13 years, just male in the two schools were chosen for the study. To select the study subjects, the students were first classified according to their educational level (grade 2 to 5 basic school) and they were taken from each class category by random sampling

Inclusion and Exclusion criteria

School children different ages were included in the study.

Children who received treatment of parasitic infections during the last two weeks before the study were excluded.

Sample size:

A total of 200 urine samples were collected from the participants by systemic random sampling technique.

Ethical consideration:

The study proposal received ethical approval from the Ministry of Health and Ministry of Education, then administrations of the schools. Study aims were well explained to both schoolchildren and their parents.

Samples Collection:

Before samples were collected, children were given guidance on how to collect the sample and amount of urine needed. They were also guided not to contaminate urine with water and wash their hands afterwards. The study subjects were provided with sterile plastic, dry and clean well labeled screw capped containers and instructed to include the terminal urine needed. Then, the samples were transferred to the parasitology laboratory in University of El Imam El Mahdi for parasitological examinations.

Examination of samples:

The urine samples were examined by urine strips, centrifugation sedimentation, and filtration technique.

Examination of urine by strips:

A reagent AMP urine strip was carefully dipped into the sterile bottle containing the urine for 5 seconds. The resulting change in color of the strip was compared with manufacturer's color chart to estimate the amount of (protein, blood) in the urine.

Filtration Concentration Technique:

Urine samples were analyzed according to Pugh (1978).[17-20]

Using a standard filtration technique. A 13cm Nucleopore polycarbonate filter paper was inserted in the filtration unit. After shaking, the urine sample (10 ml) of it was withdrawn with the help of a syringe and injected into filtration unit. After filtration, the filter paper was carefully removed using a pair of forceps and placed on glass slide then covered with cover glass. Examined systematically under the microscope at ×10 magnification. All the eggs were counted and the result was recorded as parasite load and expressed as number of eggs per 10 ml (number of egg/10 ml) of urine.

Data Collection:

The studied population and the primary data were subjected to standardize questionnaire interview with specific design.

Data Analysis:

All statistical analysis was carried out by using Graph Pad prism 5 software. The one - way ANOVA and student t-test was employed for analysis of differences between groups.

$p < 0.05$ considered significant.

Out of 200 urine samples examined, the total prevalence of *S.haematobium* infection was 24%. The prevalence of infection with *S.haematobium* was 25%. According to age in Abo Bakr Alsadig school from100 samples examined, As shown in the **table 1**

Results:

Table 1: The prevalence of urinary schistosomiasis infection according to age in Abo Bakr Alsadig School:

Age group	No. sample	No .infected	No .uninfected
8-10	50	16 (32%)	34 (68%)
11-13	50	9 (18%)	41 (82%)

The prevalence of infection with *S.haematobium* was 23% according to age in Khalid Ibn Al walid school from100 samples examined, as shown in **table 2**.

Table 2: The prevalence of urinary schistosomiasis infection according to **age in Khalid Ibn Al Walid School:**

Age	No. sample	No .infected	No .uninfected
8-10	50	10(20%)	40 (80%)
11-13	50	13 (26%)	37 (74%)

Discussion:

In Sudan, Prevalence of intestinal and urinary schistosomiasis among school children continues to be a major public health problem[21,22].

The urinary schistosomiasis in children causes chronic infections which can negatively affect all aspects of children health, nutrition and learning

Schistosomiasis infection during childhood cause substantial growth retardation and anemia. Also cause structural abnormalities of urinary tract. It the most common cause of hematuria in countries where the disease is endemic. [23- 26]

The bladder, lower ureters, urethra, seminal vesicles, uterus, cervix, and vagina were the sites usually affected. [27]

The main presenting features of urinary schistosomiasis are painful terminal hematuria, loin pain, and symptoms of secondary bacterial infection[28-31].

State Symptoms associated with genital

The prevalence of the disease was found to

Schistosomiasis are dysmenorrheal, menorrhagia, leucorrhea, lower abdominal pain, and intermenstrual bleeding. [32]

From the results, urine samples collected for urinary schistosomiasis given a prevalence of 24% of which 12.5% was reported from the Abo Bakr Alsedig School (far and 11.5% from Khalid Ibn Al Walid School. The prevalence is slightly higher in Abo Bakr Alsedig when compared with Khalid IbnAl Walid this variation is not statistically insignificant but the prevalence rate may higher due to drinking water of (Hafir) and many displaced people in the school of Abo Bakr Al Sedig. In the school of Khalid Ibn Al Walled is less common because of the drinking water of the pipes. According to several previous studies White Nile, lower in Al Liya area (Kosti) and in Gos

Alsaalaam area (Kosti). Compared with the (Hussien2016), and (Ahmed2006),

be Present study, the prevalence of infection with urinary schistosomiasis in Algablin village is higher than prevalence in (El Tawella, Al Liya, and Gos Alsaalaam), this may be due to the presence of displaced people in the studied area and may also be attributed to the drinking water sources**.**

Conclusion:

The study concluded that the prevalence of *S.haematobium* parasite infection is 24% in the studied area, and that the prevalence of urinary schistosomiasis was higher in age group 8-10 years than age group 11-13years. Not how the school near or far from the river and the use of the toilets shows importance with regard to urinary schistosomiasis. But education and sources of water used for drinking or swimming was significantly correlated

Recommendation:

Improving the hygiene through good sanitation and provision of latrines reduces water contamination. Mass treatment should Should be eradicating the infection rate in the studied area. The study advised to implement more schistosomiasis control strategies to reduce the prevalence.

It is Necessary to develop appropriate interventional programs for controlling schistosomiasis, targeting the people in White Nile State. More health education programs should be held to teach the people how to avoid schistosomiasis. Snail control should be carried to get rid of vector and to cut the disease life cycle. More prevalence studies were needed throughout the country as well as the White Nile State to provide information about the schistosomiasis.

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Original Articles

Effect of Ramadan Fasting on Psychological Status Among Healthy Sudanese Adults Living in Khartoum State

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Abstract:

Background: Ramadan month Fasting is one of the pillars of Islam and it has been found to have different physiological effects. The psychological status is related to spiritual satisfaction and the associated social interaction. Psychological well-being includes the ability to maintain a sense of autonomy, self-acceptance, personal growth, purpose in life and self-esteem.

Objectives: The aim of the study is to assess the relationship between Ramadan fasting and psychological condition of Muslims.

Methods: A cross sectional study was carried out during May to October 2019 on 82 healthy Sudanese adults living in Khartoum state. All participant were assessed by Warwick Edinbreg Mental Well Being Scale (WEMWBS). A questionnaire was filled before Ramadan and during mid of Shawal, the month after Ramadan. Data was analyzed using SPSS version 25. P-value considered significant if it is < 0.05.

Results: There was a significant change in the WEMWBS before and after Ramadan with mean of (58.2) ±.139 S.D and (59.5) ±.153 S.D respectively and (P value = .000).
Conclusion: The study showed that Ramadan Fasting improves psychological condition in normal adults.Tarawih has spiritual impact on Muslims' lives**.**

Key words: Ramadan fasting, psychological condition, WEMWBS, Khartoum.

Introduction:

Ramadan is the 9th month of the Higri year and its fasting is obligatory for healthy adult Muslims.[1] The duration of fasting is about 14 hours a day from sunrise to sunset and it varies according to the geographical area and season in which Ramadan falls.[2] Night prayer (Tarawih) is a special prayer of Ramadan which is performed in mosques. This has a spiritual impact on Muslims which can affect their relation with each other and their psychological well-being.[3] The effects of Ramadan fasting on body functions have been studied extensively. Olgan has studied the effect of Ramadan fasting on diabetic patients; their metabolic control, attitude towards the disease and HbA_{1c} level with positive impact on these measures. Diabetes Attitude Scale (DAS) was developed by national diabetes commission in USA and is used as a reliable measure of concordance in patients with diabetes. Attitude scores of all diabetics towards diabetes were identified to be negative and state of well-being was in the middle level. The measure includes 34 questions put in 1 to 5 score. If the score is >3 it shows a positive response and if it is <3, it shows a negative response. [4]

Psychological well-being include the ability to maintain a sense of autonomy, self-acceptance,personal growth, purpose in life and self esteem. Staying mentally healthly is more than treating or preventing mental illness.[7] Researshers in Warwick and Edinburgh developed a scale to enable measuring the mental well-being and they named it as Warwick-Edinburgh Mental Well-being Scale (WEMWBS).[7] **(table 1**) show it.

WEMWBS is a 14 item scale of mental well-being covering subjective well-being and psychological functioning in which all items are worded positively and address aspects of positive mental health. The scale is scored by summing responses to each item answered on a one to five Likert scale. The minimum score is 14 and maximum is 70 (**table 1**).[7]

A study was done to know the effect of Ramadan fasting on the facial expession and an emotional expression and it showed that self-measurement of mood incresed during the fasting period also they studied the behaivor and event releated potential and the data analysis indicated that the neural dynamic are different in fasting and facial expressions are more happy which increase the right hemisphere activation than the left. [8]

In one study, it has been found that Ramadan fasting decreases both frequency and duration of migraine attacks inspite of decreased caffeine and medications.[9]

It showed in another study that Ramadan had positive influence on performance in the domains of psychomotor function /processing speed and attention. The results exhibited a marked decrease in values of diastolic blood pressure during Ramadan also slower response times and performance decrements were observed.[10]

In 2018 Amani and Musa conducted a study to assess the relationship between fasting, body mass index and blood pressure in which they found that there was significant decrease in weight and body mass index after Ramadan fasting.[11]

Methods:
A cross Sectional study was conducted in 82 adult subjects (28 males and 54 females) durring the period (May-October 2019) in Khartoum and their ages range between 16 to 8o years old and not known to have any psychological problems and fasting ramadan (people who are psychlogically normal but not fasting ramadan due to any cause not included in the study).

Aim of the study was explained to all participants and a consent was obtained from each. An ethical approval was issued from the National Ribat University, Faculty of Medicine. All participants were interviewed 3 times by a questionnaire which included age, marittal status, assessment of psychological condition by WEMWBS (**Table.1**), reading Holy Quran, Tarawih prayer and thinking about marriage during fasting. The first time before Ramadan, the second in The last ten days of Ramadan and the third at mid of Shawal.

Data Analysis:
Statistical analysis was performed using SPSS version 25.0. Proportions of the studied groups were expressed in percentages and means were used to describe the studied variables, P value ≤ ,05 was considered significant.

Table (1): Shows the Scoring of WEMWS[7]

Statement	None of the time	Rarely	Some of the time	Ofte n	All of the time
	1	2	3	4	5
I've been feeling optimistic about future					
I've been feeling useful					
I've been feeling relax					
I've been feeling interested in others					
I've had energy to spare					
I've been dealing with problems well					
I've been thinking clearly					
I've been feeling good about my self					
I've been feeling close to other people					
I've been feeling confident					

I've Make up my own mind about things					
I've been feeling loved					
I've been interested in new things					
I've been feeling chearful					
Scores					

Results:

The demographic data is shown in **table (2)**. The age of participants was divided into two groups young adults and elderly 70.7% of participants within the age group of 16-35 years and 29.3% in the age group of 36-80 years old. Concerning the gender of the participants, 65.7% of participants were females and 34.1% were males. 61% of the studied sample at university level, 19.5% at secondary school, 15.9% post graduate degree and 3.7% at primary level. 48.8% were married while 50% were single.

The mean of WEMWBS before and after Ramadan was 58.2 ±.139 S.D and 59.5 ± .153 S.D, respectively (p value = 0.00) (**figure1**).

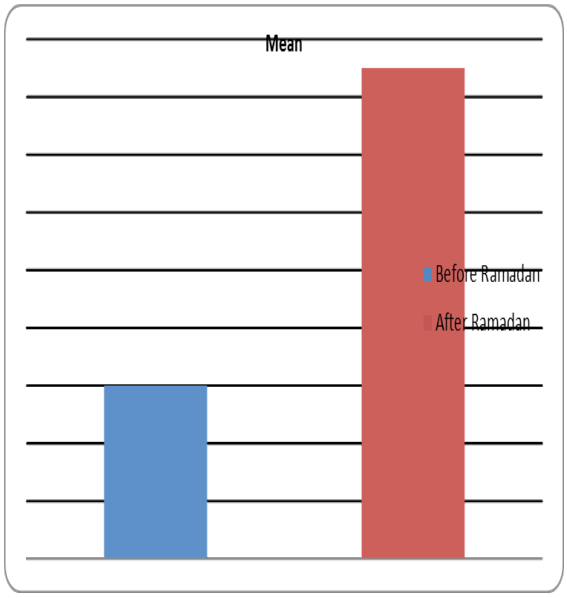

Figure (1): Shows changes in mean of WEMWBS before and after Ramadan Fasting (N=82).

Table (2): Shows mean Standard Deviation and Standard Error of WEMWBS before and after Ramadan Fasting (N=82)

Test	Mean	S.D	S.E
Pre ramadan	**58.2**	**.139**	**.017**
Post ramadan	**59.5**	**.153**	**.016**

Table (3): Shows demographic data: Gender, age, marital status and educational level (N=82)

Variable	Category	Frequency	Percentage
Gender	Males	28	34.1%
	Females	54	65.7%
Marital status	Single	41	50%
	Married	40	48.8%
Age group	16-35	58	70.7%
	36-80	24	29.3%
Educational level	Primary	3	3.7%
	Secondary	16	19.5%
	University	50	61%
	Post Graduate	13	15.9%

T**able (4):** Shows WEMWBS before and after Ramadan (N=82)

No	Question	Pre Ramadan Mean	Post Ramadan Mean	P value
1	I've been Feeling optimistic about future	2.26	2.43	0.000
2	I've been feeling useful	4.29	4.41	0.021
3	I've been feeling relaxed	3.62	4.10	0.058
4	I've been feeling interested in other people	4.15	4.38	0.001
5	I've had energy to spare	4.28	3.80*	0.004
6	I've been dealing with problems well	4.23	4.24	0.003
7	I've been thinking clearly	4.37	3.74	0.000
8	I've been feeling good about my self	4.13	4.37	0.001
9	I've been feeling close to other people	4.12	4.44	0.021
10	I've been feeling confident	4.41	4.56	0.000
11	I've make up my own mind about things	4.68	4.63*	0.002
12	I've been feeling loved	4.21	4.35	0.000
13	I've been nterested in new things	3.82	4.21	0.003
14	I've been feeling chearful	3.83	3.92	0.001

The mean in all questions in WEMWBS increases after Ramadan than before except for questions 5,7 and 11 in the table above.

Discussion:

Ramadan fasting is of great spiritual value in a Muslims' lives nd imposes a huge change in their life style and spiritual activities which are special for Ramadan. Its effects on the body systems have been studied[5,6] but its psychological impact was taken as guranteed and it needs more studies.

The WEMWBS was structured to study the mental well-being of the population and it has elements related to the psychological status. From the sclae,the questions 1-4,8-10 and 12-14 have shown positive improvement after Ramadan fasting, which indicates the positive impact of Ramadan fasting on the psychological status. The questions which have shown negative responses after Ramadan are only three (5,7&11) and they are related to the physical and mental activities which can be

explained by the unusual hectic traditional activities during Ramadan in Sudan.
In this study Ramadan Fasting improves the psychological condition of participants. This finding is in agreement with wael. [9] and Abdulrahman studies.[10] Tarawih has its effect to improve psychological status.

Conclusion and recommendations:

The psychological score even before Ramadan in Sudanese is good and further improved after Ramadan fasting. We recommend to use psychological score in psychologically ill people to see the effect of Ramadan fasting among them, and another study is needed to see the psychological effects in those who do not fast for accepted reasons.

Conflict of interest: No conflict of interest.

Acknowledgment

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Original article

The Effect of drinking water chlorine concentration on thyroid gland in White Nile State population (Sudan).

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Abstract:

Introduction: Thyroid disease may be one of the most common diseases in the world. That affects more than 200 million people worldwide. According to current World Health Organization "W.H.O." statistics more than 3 billion people in the world live in iodine deficient countries.

Objectives:

To know the effects of chlorine concentration of the drinking water on the thyroid functions of populations of Kosti city- Sudan

Material & Methods:

This is a prospective study which was conducted during the period October 2017 to December 2018 in Kosti city-White Nile state in Sudan. Thirty nine of Sudanese families participant with thyroid gland disorders were involved in this study. Drinking water samples were collected in sterile plane containers from different area of White Nile (center and beach) and from Kosti drinking water net. Chlorine concentrations levels in drinking water measured by using titration test (**Mohr's Method**). Venous blood samples were collected from participants for measuring the thyroid hormones levels from the serum by using ichroma™ II (immune analyzer-Boditech company). Data were recorded, collected and then analyzed using mean and standard deviation test by SPSS software, version 16.0.

Result:

Concentrations of chlorine in White Nile water as fallow: from center was 12.8 ppm and from beach was 14.2 ppm and for tap water from kosti drinking water net was 9.6 ppm. All participants in this study were females with a mean age of 38.08±14.3years . The mean of serum free T3 levels was 2.4±0.6pg/ml , the mean of serum free T4 levels was 4.7±4.8pg/ml and the mean of TSH levels was 1.05±0.8pg/ml.

Conclusion:

Chlorine concentration in White Nile and Kosti –city drinking water net is higher than levels recommended by WHO. Chronic exposure of drinking water with high concentration of chlorine contributes to development of goiter and impaired thyroid function.

Keywords: Drinking water chlorine, thyroid gland

Introduction:

Thyroid disease may be one of the most common diseases in the world. That affects more than 200 million people worldwide. According to current World Health Organization "W.H.O." statistics more than 3 billion people in the world live in iodine deficient countries.[1] The most common presenting clinical features of thyroid disease are the result of hypothyroidism, hyperthyroidism and goiter.

Hypothyroidism affects between 3% and 10% of adults, with incidence higher in women and the elderly.[1] In Africa, goiter is endemic in several countries, notably Congo, Uganda, Kenya, and Sudan; the prevalence of goiter is as high as 81% in some parts of these countries.[2] In Sudan, endemic goiter and iodine deficiency disorders are serious health problems in many areas. The incidence of goiter among schoolchildren was estimated to be 85% in the Darfur region in western Sudan, 74% in the Kosti area, 13.5% in Port Sudan in eastern Sudan, and 17% in the capital, Khartoum.[3] Prevalence of thyroid nodules is elevated in women in areas of iodine deficiency and increases with advancing age. [4] Little is known about the prevalence of goiter in other areas of Sudan. In the areas studied so far, iodine deficiency was known as the principal etiologic factor. Though, consumption of pearl millet, vitamin A deficiency, and protein-energy malnutrition were also suggested as instrumental factors in the etiology of endemic goiter in western Sudan. [5,6]

Chlorine is the most commonly used disinfectant and oxidant in drinking-water treatment. In water, chlorine reacts to form hypochlorous and hypochlorites. The Na / I symporter (NIS) is an integral plasma membrane glycoprotein that mediates active iodide transport into the thyroid follicular cells. NIS-mediated iodine accumulation in the thyroid is an active transport process that occurs at the

basolateral plasma membrane of the thyroid follicular cells against the iodine electrochemical gradient, stimulated by TSH and inhibitable by the well-known classic competitive inhibitors thiocyanate (SCN) and perchlorate (ClO4).[7] Iodine is then translocated from the cytoplasm across the apical plasma membrane toward the colloid in a process called iodine efflux, which has been proposed to be mediated by pendrin (aCl/I transporter) , in a complex reaction at the cell-colloid interface, called organification of iodide and catalyzed by thyroperoxidase (TPO), iodine is oxidized and incorporated into some tyrosyl residues within the thyroglobulin (Tg) molecule, leading to the subsequent coupling of iodotyrosine residues. The term organification refers to the incorporation of iodine into organic molecules, as opposed to non incorporated, inorganic, or free iodine.[7] Perchlorate (ClO4) is an anion that competitively blocks iodide from entering the thyroid by an effect on the sodium/iodide symporter (NIS) thus preventing the further synthesis of thyroid hormone but has no effect on thiodination process itself, it reduces thyroid hormone synthesis and circulating levels of thyroid hormones.[8] Therefore, perchlorate is expected to produce deleterious effects on an organism solely by reducing thyroid hormone synthesis and release. And causes goiter and hypothyroidism symptoms.[8]

Drinking water disinfection is a process or a series of processes intended to inactivate human pathogens such as viruses, bacteria and protozoa, potentially present in influent water before the water is delivered to the first consumer. Effective disinfection of adequately filtered influent water or raw water of suitable quality can be accomplished by either chemical or physical means such as the use of chlorine, chlorine dioxide, ozone or ultraviolet light. However, the disinfection processes will not be as effective on influent waters of inferior quality.[9,10]

There are many disinfectants, iodide can modifying by them, as well as its possible implication in altering thyroid function, should be rationalized in terms of the biological role of the monovalent anions of the group VII elements, which consists of five chemically related elements: fluorine (F), chlorine (Cl), bromine (Br), iodine (I), and astatine (At)[11]: Fluoride (F^-) is essential for mineralizing bone matrix and dental enamel. It is not present in body fluids in significant quantities. Fluoride is toxic when present in body fluids in detectable quantities. Chloride (Cl^-) is the ubiquitous essential anion for electrolyte balance and is present in body fluids in decimolar quantities. It is secreted by the gastric mucosa as free acid in excess of physiologic concentrations. Bromide (Br-) is a toxic and xenobiotic anion. It is not normally present in body fluids. Iodide (I) is essential for thyroid hormones synthesis and basal metabolism. It is concentrated in thyroid gland, salivary glands, and parietal cells. Iodide is present in body fluid in, micromolar (μM) quantities. It is secreted in saliva and gastric juices and inhibits thyroid function at higher than required doses. Astatite (At-) is a rare and unstable anion of no biological significance.[11]So from the above information chlorine widely and safely used as water disinfectant.

The aim of this study:

To know the effects of the drinking water chlorine concentration on the thyroid functions of populations of Kosti city-Sudan

Material & Methods:

Thirty nine of Sudanese families participant with thyroid hormones disorders were involved in this study. The study was conducted during a period from October 2017 to December 2018 in Kosti city-White Nile state in Sudan. Patients with thyroid hormones disorders (Hypo-thyroidism, hyperthyroidism and goiter) were included in this study. Patients who have thyroid disorders with diabetes, cardiovascular disease, liver disease, alcoholism, smoking, taking of any

vitamins and minerals and patients with thyroid hormones disorders under treatment were excluded from this study.

Ethical consideration:
Permission of this study was obtained from the local authorities. A written consent were obtained from each participant in this study.

Samples processing:
Water samples:
Drinking water samples were collected in sterile plane containers from different area of White Nile (center and beach) and Kosti drinking water net. Chlorine levels measured by using titration test (Mohr's Method)

Procedures:
Titration test:
Titration test using Silver nitrate and Potassium Chromate. 0.01 M (molar)of Silver nitrate and 0.05g /l(gram / litter) of Potassium Chromate.

Mohr's Method:
In the Mohr's method the determination of the end point is based on the formation of a second precipitate which is colored. The requirement here is that the second precipitate should have solubility slightly greater than the precipitate between the analyze and the titrant. The indicator used is potassium chromate and the second precipitate formed is brick–red colored silver chromate, Ag2CrO4.[12]

Blood samples:
Venous blood samples were collected in plane containers and we measured thyroid hormones levels from serum by using ichroma™ II (immune analyzer-Boditech company) All selected participants was interviewed and filled a questionnaire form including information about personal data, smoking habits, Family history of thyroid diseases, past medical history of chronic illness, drug history that interfering with thyroid functions.

Statistical data analysis:
Data were recorded, collected and then analyzed using mean and standard deviation test by SPSS software, version 16.0.

Results:
The concentrations levels of chlorine for White Nile water were determined as follows. Concentration of chlorine for center was 12.8 ppm (**Table 1**),for beach was 14.2 ppm (Table 2) and for tap water from kosti drinking water net was 9.6 ppm (**Table3**). All values are higher concentration according to WHO guide lines of chlorine concentration for drinking water (5mg/l). All participants in this study were females with a mean age of 38.08±14.30 years.
The mean of serum free T3 levels was 2.4±0.6pg/ml , the mean of serum free T4 levels was 4.7±4.8pg/ml and the mean of TSH levels was 1.05±0.8pg/ml (**Table-4**). Twenty one (53.3%) of participants had an euthyroid goiter, 7 (18%) of participants had hyperthyroidism and 11(28.2%) of participants had hypo-thyroidism. The mean of goiter duration was 1.44 ±0.5 year.

Table (1) :chlorine concentration of White Nile(center)

Area	No of test	Initial volume of AgNO3	Final volume of AgNO3	Volume used of AgNO3	Chlorine concentration
Center	1	0	3.5	3.5	
	2	3.5	7	3.5	12.8ppm

Table (2) :chlorine concentration of White Nile (beach)

Area	No of test	Initial volume	Final volume	Volume used of	Chlorine

		of AgNO3	of AgNO3	AgNO3	concentration
Beach	1	16	20	4	
	2	20	24	4	14.2 ppm

Table (3) :chlorine concentration of Tap water(Kosti city water net)

Area	No of test	Initial volume of AgNO3	Final volume of AgNO3	Volume used of AgNO3	Chlorine Concentration
Tap water	1	8.5	12.2	2.7	9.6 ppm
	2	13.3	16	2.7	

ppm= partial part of million
ppm= mg/l

Table (4): Thyroid hormones levels of the studied group

Thyroid hormone	Mean ±SD
FT3	2.4±0.6pg/ml
FT4	4.7±4.8pg/ml
TSH	1.05±0.8pg/ml

Discussion:

Chlorine concentration in drinking water in White Nile and Kosti city drinking water net were measured (center = 12.8 ppm , beach=14.2 ppm and water net=9.6 ppm) ,from this results chlorine concentration in White Nile was very high than the normal range that which recommended by WHO (Guidelines for drinking-water quality, World Health Organization 2017).[8] WHO put values of chlorine concentration in drinking water(Chlorine:5 mg/l (5000 µg) , Chlorite: 0.7 mg/l (700 µg/l)and Chlorate: 0.7 mg/l (700 µg/l). Chlorite and chlorate are resulting from the used of chlorine dioxide as a disinfectant, for odour and taste control in water.[13] So chlorine concentration in drinking water significantly affects animals and human as the same on thyroid gland functions.

In this study the mean concentration of free T3 is 2.4±0.6pg/ml (normal range 0.75-1.58pg/ml), the mean level of free thyroxin is 4.7±4.8pg/ml normal range 4.9-11.0 pg / ml. High chlorine concentration in drinking water cause reversible thyrotoxic effects in African green monkeys in short-term exposure and caused decrease in thyroxin level in male rats in dose dependent exposure [14]. In this study the mean level of free T3is little bit higher than normal range, this can explain that 18% of studies group were had hyperthyroidism. All the females in study had a goiter and had seen chronically exposed to high concentration of chlorine in their drinking water. High concentrations of chlorine in drinking water impair iodide uptake by the thyroid gland by sodium/iodide symporter (NIS) for synthesis of the thyroid hormones. Chlorine acts as an inhibitor of the sodium-iodine symporter (NIS) by binding to NIS impairs thyroid iodine uptake, impacting on the normal functionality of the gland, with particular focus in identifying the sub-population at higher risk for thyroid disruption.[15]

The majority of human data are clinical reports of patients treated with potassium perchlorate for hyperthyroidism resulting from Graves disease, an autoimmune condition. The mode of action for perchlorate toxicity is the competitive inhibition of iodide anion uptake by the sodium-iodide symporter, a carrier protein

responsible for the active transport of iodide across the basolateral membrane of the thyroid epithelial cells.[16]

Thyroid hormone synthesis is inhibited resulting in deceased levels of T3 and T4, increased TSH levels, and stimulation of thyroid cell proliferation. In addition, some data suggest that perchlorate causes a release of accumulated iodide from the gland [17,18]. All participants in this study were females who developed a goiter of various sizes. Similarities in thyroid histopathology between perchlorate and chlorate exposure suggest that chlorate may interfere with iodide up-take as well, resulting in stimulation of thyroid follicular cell proliferation mediated by TSH secondary to decreases in T3 and T4. [19] So high level of chlorine in drinking water impaired the production of thyroid hormones from gland and this low level of thyroid hormones stimulates the pituitary gland to release the thyroid stimulating hormone (TSH) which leads to hyperplasia and hypertrophy of thyroid gland and development of goiter.

We conclude that chlorine concentration in White Nile and Kosti–city drinking water net is higher than levels recommended by WHO. Chronic exposure of drinking water with high concentration of chlorine contributes to development of goiter and impaired thyroid function.

We recommend the following measurement in order to improve the quality of the drinking water and to reduce the toxic effect of chlorine on thyroid gland in white Nile state: Using an alternative methods of drinking water disinfection like ultraviolet, ozonition and boiling in order to reduce the toxic effect of chlorine on thyroid gland. Establishment of screening programs for thyroid gland diseases among people in areas where treatment of drinking water done by chlorination or the water itself has high concentration of chlorine. More researches and studies were needed to see the effects of drinking water disinfectant on human thyroid gland.

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Review Article

Covid 19 Pandemic: The little We Know

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Abstract

Corona virus disease 19(COVID19) is single-stranded RNA virus, belonging to the family Corona viridae, which can cause various diseases with enteric, respiratory, hepatic and neurological symptoms.

2019-nCoV is characterized by strong contagion, high morbidity and high mortality, but no specific drugs of 2019-nCoV have been developed so far . Started in wuhan late in 2019 and spread throughout the world, in March 2020 the WHO declare COVID 19 pandemic.

The disease spread from animals to persons or from person to person through droplets or air or contaminated surfaces. The patient can transmit the disease in the incubation period and became more infectious as they develop symptom, the duration of infectivity is variable and depends on the disease severity.

Antibodies to the virus are induced in those who have become infected and there is evidence it is protective as convalescent plasma for treatment of COVID-19 identified neutralizing activity in plasma of recovered patients that appeared to be transferred to recipients following plasma infusion.

Personal preventive measures are used to reduce the risk of transmission e.g. distancing, hand wash, avoid touching face, respiratory hygiene and Cleaning and disinfecting objects . The incubation period is 2-14 days and it has respiratory symptoms like cough and shortness of breath and wide range of non respiratory symptoms e.g. gastrointestinal like abdominal pain, diarrhea, nervous system ischaemic or haemorrhagic stroke, dizziness, headache, anosmia, musculoskeletal disturbance, altered mental state, Guillain-Barré syndrome, or acute necrotizing encephalopathy. Cardiac like acute coronary syndrome and carditis also reported.

Disease severity varies from mild disease, pneumonia, severe pneumonia, acute respiratory distress syndrome, sepsis or septic shock.

Diagnosis is based on the clinical presentation in addition to radiological evidence of consolidation and reticulo-nodular shadowing in chest X ray and or CT chest and the polymerase chain reaction

Management is supportive care boosting the immunity in mild cases, several drugs are under assessment including antiviral drugs like Remdesivir which is a novel nucleotide analogue, Tocilizumab an Interleukin 6 (IL6) inhibitor, dexamethasone increase survival in critically ill patient who need supported ventilation and critical ill patient may need assisted ventilation. Researches on vaccination are running and the result are awaited.

Keywords: Covid 19, Pandemic, Airborne,Transmission, Immunity, Prevention

Introduction:

Corona viruses are single-stranded RNA viruses belonging to the family Corona viridae, which can cause various diseases with enteric, respiratory, hepatic and neurological symptoms. Corona virus comprises of a large family of viruses that are common in human beings as well animals (camels, cattle, cats, and bats). There are seven different strains of corona virus, 229E (alpha corona virus), NL63 (alpha corona virus), OC43 (beta corona virus), HKU1 (beta corona virus), MERS-CoV (the beta corona virus that causes Middle East Respiratory Syndrome, or MERS), SARS-CoV (the beta corona virus that causes severe acute respiratory syndrome, or SARS) and SARS-CoV-2 (the

novel corona virus that causes corona virus disease 2019, or COVID-19). [1]

Objective:

To provide up-to date information about corona virus 19 pandemic; diagnosis, clinical presentation, prevention, and vaccination.

Epidemiology:

The new corona virus denoted as the 2019 novel corona virus (2019-nCoV) or corona virus disease 2019(COVID-19) first reports of cases from Wuhan, at the end of 2019 it soon becomes of extreme worldwide concern. It leads to a significant outbreak in many regions in China and expands globally since then, the spread of covid-19 has increased and the World Health Organization declaring a pandemic on 11 March, it affects 30.3 million and lead to 948.000 deaths worldwide up to the 19th of September 2020.[2]

Transmission:

The virus can be transmitted from animals to human beings, and from person to person via droplets while talking, coughing or sneezing; or from touching contaminated surface followed by touching mouth, eyes or nostril. The droplets typically do not travel more than six feet (about two meters) SARS-CoV-2 can be transmitted through the airborne route. SARS-CoV-2 grown in tissue culture remained viable in experimentally generated aerosols for at least three hours.[1]

Reflecting the current uncertainty regarding transmission mechanisms, recommendations on airborne precautions in the health care setting vary by location; airborne precautions are universally recommended when aerosol-generating procedures are performed. Infected individuals are more likely to be infectious in the earlier stages of infection and when they are symptomatic, viral RNA levels from upper respiratory specimens appear to be higher soon after symptom onset compared with later in the illness.[3-7] The virus was isolated from naso / oropharyngeal and sputum specimens during the first eight days of illness, but not after this interval, despite continued high viral RNA levels at these sites.[5]

Transmission of Covid19 from asymptomatic individuals (or individuals within the incubation period) was documented.[8-14]

Other possible modes of transmission:

The virus may also be present in feces and could contaminate places like toilet bowls and bathroom sinks. [15]

Detection of Covid 19 RNA in blood has also been reported in some studies [16,17,16,19] but blood borne transmission through blood products or needle sticks appears low; respiratory viruses are generally not transmitted through the blood borne route, and transfusion-transmitted infection has not been reported for SARS-CoV-2 or for the related MERS-CoV or SARS-CoV. [20]

Duration of infectivity is also uncertain, but available data suggest that prolonged viral RNA shedding after symptom resolution is not clearly associated with prolonged infectiousness. The duration of viral RNA shedding is variable; there appears to be a wide range, which may depend on severity of illness.[5,18,21-23] tests were positive for longer in patients with more severe illness[21]. However, detectable viral RNA does not always correlate with isolation of infectious virus, and there may be a threshold of viral RNA level below which infectivity is unlikely. In mild COVID-19 infectious virus was not detected from respiratory specimens when the viral RNA level was $<10^6$ copies / Ml.[5] Patients continue to have detectable viral RNA in upper respiratory samples following clinical recovery, three days after recovery the RNA concentrations are generally at or below the levels at which replication-competent virus can be reliably isolated; additionally, isolation of infectious virus from upper respiratory specimens more than nine days after illness onset has not yet been documented. [24] Infectious virus

has also not been isolated from respiratory specimens of patients who have a repeat positive RNA test following clinical improvement and initial viral clearance. [25]

Immunity and risk of re-infection:
Antibodies against the virus are induced in those who have become infected.
Preliminary evidence suggests that some of these antibodies are protective . Moreover; it is unknown whether all infected patients mount a protective immune response and how long any protective effect will last.[26]
Data on protective immunity following COVID-19 are emerging.[4,5,26]

A case series evaluating convalescent plasma for treatment of COVID-19 identified neutralizing activity in plasma of recovered patients that appeared to be transferred to recipients following plasma infusion. [26] Studies evaluating SARS-CoV-2 vaccine candidates in macaques have also suggested that immune responses to vaccination result in lower levels of viral RNA in respiratory tract specimens following viral challenge compared with unvaccinated controls.

Prevention:
Infection control in the health care setting:
Personal preventive measures: If community transmission of SARS-CoV-2 is present, residents should be encouraged to practice social distancing by staying home as much as possible and maintaining six feet (two meters) distance from others when they have to leave home. In particular, individuals should avoid crowds and close contact with ill individuals.

The following general measures are additionally recommended to reduce transmission of **infection**: Diligent hand washing, Use of hand sanitizer that contains at least 60 percent alcohol is a reasonable alternative if the hands are not visibly dirty. Avoiding touching the face.[27] Cleaning and disinfecting objects and surfaces that are frequently touched.
Individuals who are caring for patients with suspected or documented COVID-19 at home should also wear a face cover when in the same room as that patient (if the patient cannot wear a face cover). Individuals who develop an acute respiratory illness (e.g, with fever and/or respiratory symptoms) should be encouraged to self-isolate at home (away from other individuals and pets in the household) for the duration of the illness and wear a face cover if they have to be around other people.[28]

Incubation period:
The incubation period is variable between 2 to 14 days after exposure, with most cases occurring within 5 days after exposure [29-31]
Clinical features:
The median interval from the start of initial symptoms to significant symptom aggravation like dyspnea or appearance of acute respiratory distress syndrome is 7 days, ranging from 1 day to 20 days. According to pneumonitis diagnosis and treatment plan for corona virus infection, severe patients often have dyspnea and/or hypoxemia one week after the onset of the illness. Serious cases can quickly progress to acute respiratory distress syndrome, septic shock, metabolic acidosis, co-agulopathy and multiple organ failure.[32]
Severe acute respiratory illness with fever and respiratory symptoms, such as cough and shortness of breath, comprise the working case definition used to select people for viral testing,
this strategy captures typical symptomatic presentation, but imperfectly identifies unusual manifestations, such as patients without respiratory symptoms or only very mild symptoms. One widely cited modeling study concluded that up to 86% of cases might have been missed in and reports of patients with unusual presenting symptoms are rising worldwide.[33]

Non-respiratory symptoms:
The initial symptoms include fever; usually high grade occurs within several days, additionally headache and muscle pain or fatigue.[34]

Gastrointestinal symptoms and diarrhea can be the initial manifestation of infection. [35-37] Viral RNA has been detected in stool samples, sometimes at high levels [38]; this raises the possibility of feco-oral transmission.[39] Taste or olfactory disorders were noted[40] and new anosmia is being proposed as a criterion for testing, especially in young people with few other symptoms.

Other neurological symptoms among patients with covid-19, including ischaemic or hemorrhagic stroke, dizziness , headache, musculoskeletal disturbance, altered mental state, Guillain-Barre syndrome, or acute necrotizing encephalopathy, without proof of direct viral invasion into the.[31,41,42] Systematic testing for SARS-CoV-2 should be considered in patients with acute neurological events during the pandemic. Cardiovascular events that have been associated with covid-19 in preliminary observations include myocardial injury, especially in patients with severe infections, [43]myocarditis,[44]and myopericarditis with reduced systolic function[45,46], cardiac arrhythmias [47], heart failure, and misdiagnosis as acute coronary syndrome. Covid-19 was associated with a hyper-coagulable state probably increasing the risk forvenous thromboembolic events including pulmonary embolus [48] Chest pain should therefore alert clinicians to the possibility of covid-19. SARS-CoV-2 RNA could be detected in tears, ocular manifestations includes conjunctival hyperaemia, chemosis and increased secretions. [49]

Diagnostic delay has serious consequences for older adults, including increased mortality and nosocomial transmission [50]. The threshold for testing should be lowered in the vulnerable group.

The spectrum of illness severity

Mild illness: Patients with uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnoea, nasal congestion or headache. Some patients present with diarrhoea, nausea and vomiting.

Older people and immune-suppressed individuals may present with atypical symptoms.

Pneumonia: Adult with pneumonia but no signs of severe pneumonia doesn't need oxygen supplement

Severe pneumonia: Adolescent or adult: fever or suspected respiratory infection, plus one of: Respiratory rate > 30 breaths/min Severe respiratory distress $SpO_2 \leq 93\%$ on room-air .[51]

Acute respiratory distress syndrome (ARDS) Onset: within 1 week of a known clinical presentation or new or worsening respiratory symptoms.

Chest imaging (radiograph, CT scan or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules.

Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g.echocardiography) to exclude hydrostatic cause of infiltrates / oedema if no risk factor present.

Oxygenation impairment in adults:

Mild ARDS: ***200 mmHg < PaO_2/FiO_2 ≤ 300 mmHg*** (with PEEP or CPAP ≥ 5 cmH_2O, or non-ventilated)

ModerateARDS:100 mmHg< PaO_2/ FiO_2 ≤200mmHg (with PEEP ≥5 cmH_2O, or non-ventilated)

Severe ARDS: $PaO_2/FiO_2 \leq 100$ mmHg (with PEEP≥ 5 cmH_2O, or non-ventilated)

When PaO_2 is not available, $SpO_2/FiO_2 \leq$ 315mmHgsuggests ARDS.[52-54] (including in non-ventilated patients).

Sepsis: Adults life-threatening organ dysfunction caused by a dys-regulated host response to suspected or proven infection.

Signs of organ dysfunction: Altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, tachycardia, weak pulse, cold extremities or hypotension, skin mottling

Laboratory evidence of sepsis:

Coagulopathy, Thrombocytopenia, Acidosis , Raised lactate, Hyperbilirubinaemia .[55]

Septic shock:

Persisting hypotension despite volume resuscitation, requiring vasopressors to maintain mean arterial blood pressure (MAP) ≥ 65 mmHg and Serum lactate level > 2 mmol/L .[55]

Diagnosis:

Clinical finding varies between patients; mild patients may not have positive signs, while severe patients may have shortness of breath with crepitation on lungs, weakened breath sounds dullnesspercussion, enhanced or reduced tactile vocal fremitus. [20]

Chest imaging examination:

Suspected or confirmed cases should undertake chest X-ray examination as early as possible and chest CT scan is required when necessary.[56]

In the early phase of the disease, chest images show interstitial changes and multiple small plaques, especially in the lung periphery. Then the changes further deteriorate to the bilateral and are mainly distributed in the middle and outer zones of the lung with multiple infiltrating shadows and/or ground-glass opacity. Patients may have a single lobe or multiple lobes involved. When the condition gets better, a little fibrous stripe may appear.[57] Conversely, lung consolidation may occur in severe cases whose pleural effusions are rarely seen. Lung involvement was present in all cases.[58, 59] with most chest computed tomography (CT) scans showing lesions in multiple lung lobes, some of which are dense. Ground-glass opacity co-existed with consolidation shadows or cord-like shadows are observed.[60]

Laboratory examination:

Hematologic examination: nearly 80% of the patients have normal or decreased white blood cell counts, and 72.3% have lymphocytopenia.[41]

At early stage, white blood cell counts are normal or decreased, with decreased lymphocyte counts. If the absolute value of lymphocyte is less than 0.8×10^9/L, or the CD4 and CD8 T cell counts are significantly decreased, it needs high attention. [61]

In some patients, muscle enzymes, liver enzymes, and myohemoglobin levels are increased. The troponine is increased in some critical patients. Most patients display elevated erythrocyte sedimentation rate and C-reactive protein level, and normal procalcitonin levels. Severe cases show progressively decreased blood lymphocytes counts and high D-dimer levels.

Molecular diagnosis:

Real time reverse-transcription–polymerase chain- reaction (RT-PCR) is used for the diagnosis of suspected COVID 19 patients, samples collected from the upper respiratory tract (nasopharyngeal and oropharyngeal), the lower respiratory tract (expectorated sputum, endotracheal aspirate, or bronch-oalveolar lavage) , blood and feces can be used to diagnose 2019-nCoV by real time reverse-transcription–polymerase chain - reaction (RT-PCR) as well.[62] The existing PCR methods have very good specificity but low sensitivity, which means that the negative test results cannot exclude the presence of 2019-CoV in patients. Moreover ,the laboratory sample contamination caused by the lack of control can lead to the false positive results. Additionally, RT-PCR tests may be falsely negative due to insufficient viral materials or operational error. Some patients with negative results of RT-PCR may present with positive chest CT findings for COVID 19, which means PCR results can assist clinical diagnosis and evaluation but the possibility of disease cannot be confirmed or ruled out. For individuals with high clinical suspicion but negative RT-PCR screening, a combination of CT scanning and repeated swab tests may be helpful. [63]

SHERLOCK Technique:

The CRISPR-based SHERLOCK (Specific High Sensitivity Enzymatic Reporter Unlocking) technique, termed specific high-sensitivity enzymatic reporter unlocking, allows portable, multiplexed, and ultra-sensitive detection of RNA or DNA from clinically relevant samples. SHERLOCK assays are set up with recombinase-mediated polymerase pre-amplification of DNA or RNA and subsequent Cas13- or Cas12 -mediated detection via colorimetric readouts and fluorescence that provide results in less than 1 h with a setup time of less than 15 min.[64] Based on the RNA sequence of the New Coronavirus, the researchers carefully designed two guide RNAs, one that recognizes the S gene of the new coronavirus, and the other that recognizes the Orf1ab gene. In order to maximize the accuracy of the detection, scientists have selected the sequences that are most specific for the new corona virus. [65]

Pathogenic mechanism:

COVID 19 phylogenetic analysis reveals that it belonged to beta corona viruses that uses ACE2 as an entry receptor in the ACE2-expressing cells, but not cells without ACE2, and COVID 19 is likely to bind to ACE2 receptor in humans just like SARS-CoV.[66,67]

Management strategy:

Broad population screening for SARS-CoV-2 infections, isolation of confirmed cases through contact tracing and quarantine combined with social distancing, and large serological studies will be critical to slowing the spread of covid-19.

Chloroquine:

Use of chloroquine is included in treatment guidelines from China's National Health Commission and was reportedly associated with reduced progression of disease and decreased duration of symptoms.[68]

Hydroxychloroquine:

Hydroxychloroquine (200 mg tds for 10 days) was associated with a higher rate of undetectable viral RNA on nasopharyngeal specimens at day 6 compared with no specific treatment (70 vs 12.5%).

In this study, the use of azithromycin in combination with hydroxychloroquine appeared to have additional benefit, but there are methodological concerns about the control groups for the study, and the clinical basis for using azithromycin is not clear. Sudies on hydroxychloroquine stopped for savety issusues and it was withdrawn from the WHO protocols. [69]

Corticosteroids: had been widely used in management of severe acute respiratory syndrome (SARS), and low dexamethasone (6mg either by mouth or intravenous) for 10 days reduced the mortality rate in covid 19 patients by one third in critically ill patient who required ventilation and by one fifth in those who receive oxygen only and no benefit in patients who did not require respiratory support.[70]

Remdesivir:

Several randomised trials are under way to evaluate the efficacy of remdesivir for moderate or severe COVID-19.

It has activity againstSARS-CoV-2 in vitro, SARS and MERS-CoV, both in vitro and in animal studies.[71]

Tocilizumab:

Treatment guidelines from China's National Health Commission include the IL-6 inhibitor tocilizumab for patients with severe COVID-19 and elevated IL-6 levels .[72] A clinical trial is under way.

Managing asymptomatic individuals with potential exposure:

In areas where SARS-CoV-2 is prevalent, all residents should be encouraged to stay alert for symptoms and practice social distancing by staying home as much as possible and maintaining six feet (two meters) distance from others when they have to leave the home. In the United States, the CDC suggests the following approach for all residents For those returning from international travel and those who have had close contact with a patient with suspected

or confirmed COVID-19 (including during the 48 hours prior to that patient developing symptoms), the CDC also suggests

●Self-quarantine at home for 14 days following the last exposure, with maintenance of at least six feet (two meters) from others at all times.

●Avoiding contact with individuals at high risk for severe illness (unless they are household members with the same exposure). Throughout the world, countries have employed various nonpharmaceutical interventions to reduce transmission.

In addition to personal preventive measures (eg, hand hygiene, respiratory etiquette and face covers, environmental disinfection), **transmission reduction strategies include:**

●Social/physical distancing orders

●Stay-at-home orders

●School, venue, and nonessential business closure

●Bans on public gatherings

●Travel restriction with exit and/or entry screening

●Aggressive case identification and isolation (separating individuals with infection from others)

●Contact tracing and quarantine (separating individuals who have been exposed from others)

These measures have been associated with reductions in the incidence of SARS-CoV-2 infection over time, although the relative contribution of each is difficult to assess .[73]

Vaccines:

Numerous vaccine candidates are being evaluated for prevention of COVID-19 These include various types of vaccines, including nucleic acid-based (mRNA and DNA) vaccines, viral-vector vaccines, and inactivated or recombinant protein vaccines The different vaccine platforms vary in their potential safety and immunogenicity, speed and cost of manufacturing, and other features important for meeting global demand. According to WHO September 2020 nine vaccine candidates were in late stage trials the but until phase 3 is completed and the result is made available it will not be possible to make any judgment.[74]

There is also interest in Bacille-Calmette-Guerin (BCG) immunization for prevention of COVID-19, and clinical trials are underway to evaluate its use among health care workers .[75] Studies have suggested that, although its primary purpose is prevention of tuberculosis, BCG immunization induces a nonspecific immune response that may have protective effects against non-mycobacterial, including viral infections[76, 77]

Any impact of BCG immunization on COVID-19 is unknown.

The WHO recommends BCG vaccination not be used for prevention or lessening the severity of COVID-19, pending further data.[78]

Post-exposure prophylaxis: Clinical trials are also being conducted in the United States and elsewhere to evaluate the safety and efficacy of post-exposure drug prophylaxis against COVID-19. No agent is known to be effective in preventing infection; post-exposure prophylaxis should not be attempted outside a clinical trial. [79,80]

Conclusion:

Covid-19 is driving worldwide urgent public health actions and concern. Its spread is fast, with increasing numbers of infected patients, it has high morbidity and mortality and the future development of the disease is unclear. In the last year large number of researches was conducted to provide more information about the clinical features, diagnosis, mode of transmission, prevention management, and there is optimistic information about the vaccine.

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